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Kindliche Körpergerüche als Chemosignale in der Mutter-Kind-Beziehung: Integration von genetischen, hormonellen und neurobiologischen Einflüssen

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1 Zusammenfassung

Eine sichere Bindung zwischen Mutter und Kind in den ersten Lebensjahren ist prägend für die Entwicklung eines Kindes. Die Qualität dieser Bindung ist ein wichtiger Prädiktor für langfristige physische und psychische Gesundheit. Für den Aufbau einer starken Bindung ist die Investition von Ressourcen seitens der Fürsorgeperson auf zeitlicher, physischer und emotionaler Ebene notwendig. Multimodale biologische Hinweisreize seitens des Kindes fördern dieses Engagement. Zunächst dienen solche Signale der Identifikation des eigenen Nachwuchses (kin recognition), um nachfolgend gezielt Ressourcen zu investieren. Darüber hinaus können infantile Stimuli affektive Reaktionen vermitteln, die den Bindungsaufbau erleichtern. In diesem Zusammenhang sind auch olfaktorische Signale, z. B. Körpergerüche, wirksam, bislang gibt es jedoch nur wenig systematische Forschung zu ihrem Einfluss auf die Eltern-Kind-Beziehung. Einzelne Studien zeigen, dass Mütter ihre Kinder am Geruch erkennen können und dass kindliche Körpergerüche auch auf neuronaler Ebene positive Reaktionen vermitteln, wobei jedoch unklar ist, wie spezifisch die neuronale Aktivität für den Geruch des eigenen Kindes ist.

In der vorliegenden Arbeit soll der Einfluss von kindlichen Körpergerüchen in der Mutter-Kind-Beziehung über die kindliche Entwicklungsspanne unter Berücksichtigung genetischer, hormoneller und neurobiologischer Faktoren untersucht werden.

In Veröffentlichung 1 wurde geprüft, ob Mütter ihre Kinder am Geruch identifizieren können, ob sie diesen präferieren und wie beides mit genetischen und hormonellen Faktoren sowie dem kindlichen Entwicklungsstatus interagiert. Dafür wurden *N* = 164 Müttern mit ihren biologischen Kindern (*N* = 226 Kinder zwischen 0 und 18 Jahren) in die Studie eingeschlossen. Die Mütter bewerteten die Körpergerüche des eigenen und fremder Kinder, die sich im Entwicklungsstatus sowie der genetischen Ähnlichkeit unterschieden. Die genetische Ähnlichkeit wurde über das Humane Leukozytenantigen(HLA)-Profil abgebildet, der Entwicklungsstatus wurde anhand der Steroidhormonkonzentration (Testosteron, Estradiol) und einer standardisierten Einschätzung des pubertären Status erfasst. Es zeigte sich, dass die Mütter den Geruch ihres eigenen Kindes über dem Zufallsniveau identifizieren konnten und diesen Geruch präferierten. Dies galt für alle Altersgruppen, mit Ausnahme der frühen Pubertät. In diesem Alter (9-13 Jahre) konnten die Mütter den Geruch ihres Kindes weder identifizieren, noch bevorzugten sie ihn im Vergleich zu fremden Körpergerüchen. Bei den eigenen Söhnen war die Abnahme der Präferenz mit dem Anstieg des Testosteronlevels assoziiert. Mit zunehmendem Alter des Kindes (14-18 Jahre) ähnelte das Bewertungsverhalten der Mütter wieder dem vor Pubertätsbeginn, was vermuten lässt, dass die Mütter sich in diesem Zeitraum an den veränderten Geruch des Kindes gewöhnen und somit die Vertrautheit des Geruchs eine wichtige Rolle für die Wahrnehmung spielt.

Zusätzlich legen die Ergebnisse nahe, dass genetische Ähnlichkeit über Körpergerüche transportiert wird: Der Geruch des eigenen Kindes wurde zwar global bevorzugt, im paarweisen Vergleich zeigte sich jedoch, dass sich die Bewertung für den Geruch des eigenen Kindes nicht signifikant von der Bewertung des gleichaltrigen und HLA-ähnlichen Kindes unterschied. Dies lässt darauf schließen, dass sich genetische Ähnlichkeit positiv auf die Geruchsbewertung im Kontext der Eltern-Kind-Bindung auswirkt.

Für die zweite Veröffentlichung wurde anhand derselben Stichprobe getestet, ob Mütter den Entwicklungsstatus des Kindes anhand von Körpergerüchen klassifizieren können und welche Prädiktoren für die Klassifikation entscheidend sind. Dafür wurden sie gebeten, die jeweilige Altersgruppe des Kindes einzuschätzen, von dem der Geruch stammte. Die Ergebnisse demonstrieren, dass Mütter den kindlichen Entwicklungsstatus (prä- bzw. postpubertär) mit einer Genauigkeit von 64 % detektieren können und insgesamt dazu tendieren, kindliche Körpergerüche als präpubertär zu klassifizieren. Die mütterliche Klassifikationsleistung war besser, wenn die Probandinnen Geruchsproben aus der gleichen Altersgruppe wie der des eigenen Kindes beurteilten. Die subjektive Bewertung der Proben hinsichtlich Angenehmheit und Intensität sowie die Einschätzung des pubertären Status waren signifikante Prädiktoren für die entwicklungsbedingte Klassifikation eines Geruchs, während sich der Steroidhormonstatus des Kindes nicht auf die mütterliche Einschätzung auswirkte.

Die dritte Veröffentlichung dieser Doktorarbeit diente als methodische Pilotstudie für die spezifische Untersuchung des Einflusses von Babygerüchen auf die neuronale Verarbeitung im mütterlichen Gehirn. Aus anderen Modalitäten ist bekannt, dass kindliche Stimuli Niedlichkeit vermitteln, welche mit belohnungsspezifischer neuronaler Aktivität einhergeht. Dies ist für Babygerüche bisher jedoch kaum erforscht.

Die Präsentation von Körpergerüchen zur Ableitung neuronaler Korrelate im Rahmen von funktioneller Magnetresonanztomographie (fMRT) ist aufgrund von Stimuluseigenschaften sowie methodischen Schwierigkeiten herausfordernd. Bislang existieren nur wenige Studien zur neuronalen Verarbeitung von Körpergerüchen ohne einheitliche Konvention über eine geeignete Stimuluspräsentation. Im Rahmen dieser Doktorarbeit sollte daher ein effizientes Design entwickelt werden, welches neuronale Aktivität in Reaktion auf Babygerüche optimal abbildet. Dafür wurden zwei Stimuluspräsentationen verglichen, die sich in Art, Dauer und Frequenz unterschieden. Die kurze, kontinuierliche Reizdarbietung rief im Vergleich zu einer langen, gepulsten Präsentation global stärkere Aktivierungen hervor, weshalb diese als Design empfehlenswert ist, um robuste neuronale Korrelate zu erhalten. Allerdings zeigten sich differentielle Effekte in Abhängigkeit der Hirnregionen, weshalb je nach interessierendem Areal spezifisch zwischen Länge, Dauer und Art der Stimuluspräsentation

abgewogen werden sollte. Das kurze Präsentationsdesign wurde im Rahmen der weiterführenden fMRT-Studie verwendet. Diese veranschaulichte, dass Babygerüche Belohnungsareale sowie Netzwerke aktivieren, die Angehmheit, Niedlichkeit und Motivation zur Fürsorge (Pleasure-Netzwerk) kodieren. Die Aktivierungsstärke des Netzwerks sagte dabei vorher, wie angenehm die Mütter den Geruch des eigenen Babys bewerteten. Im Gegensatz zu den Verhaltensdaten aus Veröffentlichung 1, in denen sich eine klare Präferenz für das eigene Kind zeigte, konnte kein Unterschied zwischen der neuronalen Reaktion auf den Geruch des eigenen im Vergleich zu einem fremden Baby gefunden werden. Daher gilt es, die Universalität des Babygeruchs als einen Stimulus, der Niedlichkeit vermittelt, in nachfolgenden Studien systematisch zu überprüfen.

Zusammenfassend stellt diese Arbeit dar, dass kindliche Körpergerüche als Chemosignale in der Mutter-Kind-Beziehung wirken und sowohl zur Identifikation des eigenen Kindes beitragen als auch affektive Komponenten vermitteln. Außerdem wurde herausgefunden, dass Körpergerüche Informationen über genetische Ähnlichkeit und den Entwicklungsstatus des Kindes transportieren. Es bleibt offen, welche Faktoren auf molekularer Ebene tatsächlich die Veränderung des Körpergeruchs ausmachen. Chemosensorische Profilanalysen können in zukünftigen Untersuchungen Aufschluss darüber geben. Darüber hinaus sind Langzeitstudien notwendig, um die hier dargestellten assoziativen Zusammenhänge auch über den individuellen Entwicklungsverlauf abzubilden und somit Mechanismen der olfaktorisch vermittelten Eltern-Kind-Beziehung ableiten zu können. Langfristig sollen diese Informationen dazu beitragen, Strategien zur Förderung der Eltern-Kind-Beziehung zu generieren und bisher bestehende Interventionen (wie z. B. Neurofeedbacktraining) auf olfaktorische Stimuli auszuweiten.

2 Summary

A secure bond between mother and child in the first years of life is crucial for the development of a child. The quality of this bond is an important predictor of long-term physical and mental health. To create such a bond, the caregiving person has to invest resources at a temporal, physical and emotional level. Multimodal biological infantile cues facilitate this commitment. Initially, such signals serve to identify one's own offspring (kin recognition) in order to invest resources in a targeted manner. In addition, infantile stimuli can mediate affective reactions that support bonding. In this context, olfactory signals, e.g. body odors, are also effective, but so far there is little systematic research on their influence on the parent-child relationship. Individual studies show that mothers can recognize their children by their body odor and that infantile body odors also mediate positive reactions at the neural level, although it is unclear how specific they are for their own child.

The present study investigates the influence of children´s body odors in the mother-child relationship over the developmental span, integrating genetic, hormonal and neurobiological factors.

Publication 1 addressed the question of whether mothers can identify their children by body odor, whether they prefer this odor and how it interacts with genetic, hormonal factors and the child's developmental status. For this purpose, *N* = 164 mothers with their biological children (*N* = 226 children between 0 and 18 years) were included in the study and evaluated the body odors of their own and unfamiliar children, which differed in their developmental stage and genetic similarity. Genetic similarity was mapped via the human leukocyte antigen (HLA) profile, the developmental status was determined on the basis of the steroid hormone concentration (testosterone, estradiol) and a standardized assessment of the pubertal status.

The results showed that the mothers were able to identify their own child's odor above chance level and preferred this odor. This was true for all age groups with the exception of early puberty. At this age (9-13 years), mothers could neither identify the odor of their child nor preferred it to unfamiliar body odors. For the body odor ratings of their own sons, the decrease in preference was associated with an increase in testosterone level. In older children (14-18 years), maternal ratings resembled those before puberty suggesting that the mothers get used to the altered body odor of their child during this period and thus, the familiarity of the odor plays an important role for perception.

In addition, the results demonstrated that genetic similarity is transported via body odors: Although the preference for the odor of one's own child was globally observed, pairwise comparisons showed that the ratings for the own child´s odor did not differ significantly from

the evaluation of a same-aged and HLA-similar child. This suggests that genetic similarity has a positive effect on odor assessment in the context of parent-child bonding.

In the second publication, in the same sample it was examined whether mothers are able to classify the child's developmental status on the basis of body odors and which predictors are decisive for the classification. Therefore, the mothers were asked to assess the age group of the child who was the odor donor. The results revealed that mothers are able to detect the developmental status (pre- vs. postpubertal) with an accuracy of 64% and tend to classify body odors as prepubertal. The maternal classification performance was better when they rated odor samples from the same age group as their own child. The perceptual evaluation of the samples (pleasantness, intensity) as well as the assessed pubertal status predicted the development-related classification of an odor, while the child´s steroid hormone concentration had no effect on it.

The third publication of this doctoral thesis served as a methodical pilot study for the specific examination of the influence of baby odors on neural processing in the maternal brain. From other modalities, it is known that infantile stimuli transport cuteness leading to reward-related neural correlates. However, this has scarcely been investigated for baby odors so far.

Body odor presentation in functional magnetic resonance imaging (fMRI) is challenging due to stimulus properties and methodological difficulties. To date, only a few studies exist on the neural processing of body odors without a uniform convention on a suitable stimulus presentation. The aim of this thesis was to develop an efficient design that optimally maps neural activity in response to baby body odors. For that reason, two stimulus presentations were compared which differed in presentation mode, duration and frequency. The short, continuous stimulus presentation revealed stronger global activations compared to a long, pulsed presentation, thus it is recommended as a design to obtain robust neuronal correlates. However, differential effects were observed depending on the brain regions, which is why the design should be specifically adapted to the regions of interest, and length, duration and type of stimulus presentation should be considered carefully. The short presentation design was used in the follow-up fMRI study. This illustrated that baby body odors activate reward areas and a network encoding cuteness and motivation to care (pleasure network). The recruitment of this network predicted how pleasantly mothers rated their own baby's odor. In contrast to the behavioral data from publication 1, which showed a clear preference for one's own child, the neural responses did not differ between one's own or an unfamiliar baby´s odor. Therefore, the universality of baby odor as a stimulus conveying cuteness must be systematically examined in subsequent studies.

In summary, this doctoral thesis reveals that children´s body odors function as chemosignals in the mother-child relationship and mediate both the identification of the own child and

affective components. In addition, it was observed that information about genetic similarity and the child's developmental status are transcribed in body odors. It remains to be explored which factors at the molecular level actually determine changes in body odor. Future investigations using chemosensory profile analyses may clarify this question.

Beyond that, longitudinal studies are necessary in order to depict the associations presented here over the course of individual development and thus enabling the derivation of mechanisms of the olfactory mediated parent-child relationship. In the long term, this information should help to generate strategies for promoting the parent-child relationship and to extend existing interventions (such as neurofeedback training) to olfactory stimuli.

3 Einführung in die Thematik

Wie Bindung durch Geruch entsteht

Die Entstehung einer sicheren Bindung in den ersten Lebensjahren ist grundlegend für das gesunde Heranwachsen eines Menschen. Eine solche Bindung ist definiert als ein starkes, emotionales Band zwischen einer primären Bezugsperson und Kind, welches ihm Sicherheit, Schutz und Trost bietet und ihm ermöglicht, auf dieser Basis seine Umwelt zu explorieren (Bowlby, 1982; Waters & Cummings, 2000). Die Qualität der Bindung ist hierbei von großer Bedeutung. Das Erleben einer sicheren Bindung, die von Vertrauen und Verlässlichkeit gekennzeichnet ist, erleichtert stabile Beziehungserfahrungen im Erwachsenenalter (Simpson, 1990) und schafft langfristig die Voraussetzung für physische und psychische Gesundheit (Egeland & Hiester, 1995; Ranson & Urichuk, 2008; Schore, 2001). Eine unsichere Bindung ist ein starker Risikofaktor für die Entwicklung psychischer Störungen sowie für die Ausprägung ungünstiger Interaktionsstile, die mit negativen Folgen assoziiert ist (Green & Goldwyn, 2002).

Bindung entsteht durch reziprokes Verhalten, das auf Seiten des Kindes durch instinktive Signale (Schreien, Lächeln) sowie aktive Annäherung an die Bezugsperson (Anklammern, Nuckeln, Nachfolgen) gekennzeichnet ist, die in dieser wiederum entsprechende Reaktionen (Füttern, Körperkontakt) auslösen (Bowlby, 1958). Die Bezugsperson investiert dabei nicht nur finanzielle oder zeitliche, sondern insbesondere auch emotionale Ressourcen, die eine positive Entwicklung des Kindes ermöglichen (Barber, 2000). Um Ressourcen nicht zu verschwenden, sondern gezielt in den eigenen Nachwuchs zu investieren, ist es zunächst notwendig, das Kind als eigenen Nachkommen zu erkennen (kin recognition). Diese Identifikationsleistung geht mit altruistischem Verhalten einher (Burnstein, Crandall, & Kitayama, 1994). In vielen Spezies sind multimodale biologische Hinweisreize dafür verantwortlich, Familienmitglieder als solche zu identifizieren. Neben visuellen und auditiven Reizen (Kulahci, Drea, Rubenstein, & Ghazanfar, 2014; Parr, Heintz, Lonsdorf, & Wroblewski, 2010) spielen Chemosignale eine wesentliche Rolle: Insbesondere Nagetiere, aber auch Schafe nutzen olfaktorische Signale, um den eigenen vom fremden Nachwuchs zu unterscheiden (Broad, Curley, & Keverne, 2006).

Beim Menschen sind biologische Stimuli ebenfalls wichtig, um Bindungsverhalten auszulösen. Menschliche kin recognition wird z. B. über visuelle Ähnlichkeit vermittelt (Volk & Quinsey, 2007). Zusätzlich kreieren prototypische Gesichtszüge eines „Kindchenschemas“ eine universelle Niedlichkeit, die sich auf die affektive Bewertung niederschlägt (Kringelbach, Stark, Alexander, Bornstein, & Stein, 2016). Während die Bedeutung visueller und auditiver Reize für den Bindungsaufbau bereits zunehmend herausgestellt wurde (Swain, 2008), gibt

es bisher nur wenige Befunde zum Einfluss des Riechens auf die Entwicklung der Bindung zwischen Mutter und Kind. Während das olfaktorische System die wichtigste Sinnesmodalität für das Sozialverhalten von Nagetieren darstellt, ist dies im Laufe der evolutionären Entwicklung in den Hintergrund gerückt (Broad et al., 2006). Dennoch zeigen einzelne Arbeiten, dass der Geruchssinn auch beim Menschen sowohl für die kin recognition (Porter, 1998; Porter, Cernoch, McLaughlin, 1983), als auch für die Vermittlung affektiver Komponenten in der Eltern-Kind-Beziehung bedeutsam ist (Okamoto, Shirasu, Fujita, Hirasawa, & Touhara, 2016). Aus Studien zu Partnerschaft ist außerdem bekannt, dass der Körpergeruch in diesem Kontext als wichtiges Chemosignal dient, welches Attraktivität vermittelt (Sorokowska et al., 2018).

Die vorliegende Arbeit dient dazu, die Bedeutung von Körpergerüchen im Kontext der Mutter-Kind-Beziehung auf Verhaltens- und neurobiologischer Ebene zu untersuchen. Dabei sollen erstmalig die Auswirkungen genetischer und entwicklungsbedingter (hormoneller) Faktoren auf die Wahrnehmung des Körpergeruchs systematisch überprüft werden.

Riechen als Orientierungshilfe in der unbekannten Welt

Unmittelbar nach der Geburt wirken mütterliche Geruchsstoffe für Neugeborene als hochwirksame Signale, die das kindliche Verhalten leiten. Diese mütterlichen Chemosignale umfassen die Muttermilch (Loos, Reger, & Schaal, 2018) sowie den Brustgeruch, insbesondere die Sekretion volatiler Geruchsstoffe aus den Montgomerydrüsen (Doucet, Soussignan, Sagot, & Schaal, 2009). Aufgrund seiner verhaltenssteuernden Wirkung wird der mütterliche Brustgeruch sogar als das einzige menschliche Releaser-Pheromon bezeichnet (Suhle & Croy, 2019; Varendi & Porter, 2001). Das olfaktorische Hauptsystem entsteht während der ersten drei Monate der Schwangerschaft. Bereits pränatal entwickeln Babys eine spezifische Geruchswahrnehmung sowie -präferenz, die postnatal übertragen wird (Schaal, Hummel, & Soussignan, 2004; Schaal & Orgeur, 1992). Neugeborene zeigen zwei Tage postpartum eine Orientierungsreaktion zum Geruch des vertrauten Fruchtwassers (Schaal, Marlier, & Soussignan, 1995) und können ebenso ihre Mutter am Achselgeruch erkennen (Marin, Rapisardi, & Tani, 2015). Außerdem demonstrieren experimentelle Studien, dass Säuglinge eine angeborene Präferenz für Muttermilch haben, die unabhängig von bisheriger Ernährungsweise (Stillen vs. Flasche) beobachtbar ist (Marlier & Schaal, 2005). Zusätzlich weiß man, dass die Sekretion der Montgomerydrüsen die Trinkmotivation erhöht (Doucet et al., 2009).

Der Brustgeruch fördert nicht nur die orale Aktivität, sondern erleichtert ebenso die multisensorische Integration sowie die Entwicklung sozialen Verhaltens: Säuglinge, denen die mütterliche Brust präsentiert wird, öffnen stärker die Augen und weinen weniger und kürzer, wenn sie die Brust riechen können, als wenn die olfaktorische Wahrnehmung durch

experimentelle Modulation (abgeklebte Brust) verhindert ist (Doucet, Soussignan, Sagot, & Schaal, 2007). Außerdem scheint der mütterliche Körpergeruch die visuelle Kategorisierung von Gesichtern zu verbessern (Leleu et al., 2019).

Auch klinisch ist diese angeborene Geruchspräferenz relevant: Frühgeborene, die mit der Flasche ernährt werden, profitieren von zusätzlicher Exposition mit dem Geruch der Muttermilch während des Trinkens, sodass sie schneller und stärker an Gewicht zunehmen (Yildiz, Arikan, Gözüm, Taştekın, & Budancamanak, 2011). Darüber hinaus können Stressreaktionen, z. B. bei Blutabnahmen, durch mütterliche Gerüche (Milch, Körpergeruch) abgemildert werden, was sich auf Verhaltens- und physiologischer Ebene (Herzrate, Kortisolausschüttung) abbildet (Zhang, Su, Li, & Chen, 2018).

Zusammengefasst lässt sich sagen, dass der Geruchssinn einen entscheidenden Orientierungsfaktor für Säuglinge darstellt und die olfaktorische Wahrnehmung somit von Geburt an eine bedeutsame Rolle für die soziale Interaktion spielt. Im Gegensatz dazu ist Sehen und Hören zunächst weitaus weniger spezifisch und entwickelt sich zunehmend in den ersten Lebensmonaten (Johnson, 2001; Peck, 1995).

Olfaktorischer Fingerabdruck – Riechen erleichtert Bindung

Auch auf Seiten der Mutter existieren olfaktorische Mechanismen, die unmittelbar nach der Entbindung wirksam sind: Mütter können ihre Kinder in den ersten Tagen nach der Geburt am Geruch identifizieren (Porter et al., 1983) und die Wahrnehmung dieses Geruchs ist positiv mit dem anfänglichen Kontakt zwischen Mutter und Kind assoziiert (Fleming et al., 1993). Diese Ergebnisse deuten auf eine affektive Bedeutung des Körpergeruchs hin, die über die bloße Erkennung des eigenen Nachwuchses hinaus geht. Neuere Befunde zum Vergleich zwischen psychisch gesunden Mütter und Müttern einer teilstationären Stichprobe mit postpartalen Bindungsstörungen unterstützen diese Hypothese: Im Vergleich zu den Patientinnen können gesunde Mütter ihr Kind anhand des Körpergeruchs besser identifizieren und zeigen eine stärkere Präferenz für den Geruch des eigenen im Vergleich zu einem fremden Baby (Croy, Mohr, Weidner, Hummel, & Junge-Hoffmeister, 2019).

Zwei Studien haben sich außerdem die Bedeutung von Körpergerüchen im Rahmen der Erziehung angeschaut. Dubas, Heijkoop und Van Aken (2009) fanden heraus, dass Eltern, die ihr Kind am Geruch erkennen können, weniger bestrafendes und negatives Erziehungsverhalten zeigen, als Eltern, die das nicht können. Damit einher gehen die Ergebnisse von Okamoto et al. (2016), die verdeutlichen, dass Körpergerüche sowohl instrumentelle (z. B. Windeln wechseln) als auch affektive Informationsquellen (z. B. durch liebevolles Schnüffeln) in der Erziehung darstellen und Eltern diese in der täglichen Erziehung aktiv nutzen (Okamoto et al., 2016).

Auch wenn diese Studien auf korrelativen Zusammenhängen beruhen und keine Kausalität abgeleitet werden kann, sprechen die Befunde für eine affektive Bedeutsamkeit von Körpergeruch im Kontext der Eltern-Kind-Beziehung. Diese affektive Bedeutsamkeit lässt sich am besten über subjektive hedonische Geruchsbewertung (z. B. Angenehmheit) oder neuronal vermittelte Belohnung abbilden (Lundström et al., 2013; Okamoto et al., 2016).

Neurobiologie der Riechverarbeitung

Die Verarbeitung von Geruchsreizen geschieht in mehreren Schritten. Zunächst treffen die olfaktorischen Moleküle auf Rezeptorneuronen am Riechepithel, die über die Riechbahnen zum olfaktorischen Bulbus (Riechkolben) ziehen und in den Synapsen der Glomeruli auf Mitralzellen verschaltet werden. Von dort werden diese Signale in basal-frontale und medial-temporale Hirnareale weitergeleitet (Gottfried, 2010). Alle Areale, die direkt aus dem Bulbus stammende Projektionen erhalten, werden als primärer olfaktorischer Kortex bezeichnet (Gottfried, 2006). Dazu zählen der piriforme Kortex als zentrale Struktur, die einen Großteil der Informationen empfängt und an nachgeschaltete Stellen übermittelt, sowie Amygdala und entorhinaler Kortex. Von primären Arealen ausgehend werden die sekundären olfaktorischen Strukturen erreicht, welche anteriore Insula, Hippocampus, Hypothalamus und orbitofrontalen Kortex (OFC) umfassen. Besonders an dieser Verarbeitung ist, dass die Mehrzahl der Riechreize im Vergleich zu anderen sensorischen Stimuli nicht zuerst über den Thalamus verschaltet, sondern direkt in sekundäre Strukturen projiziert werden. Außerdem verdeutlicht die unmittelbare Weiterleitung in das limbische System die evolutionäre Bedeutsamkeit des Riechens für die menschliche Entwicklung (Gottfried, 2006) und erklärt die starke Kopplung von Gerüchen mit Gefühlen sowie Erinnerungen (Herz, 2004). Die subkortikale Lage der Riechstrukturen erschwert die präzise Abbildung neuronaler Korrelate olfaktorischer Verarbeitung aufgrund von Suszebilitätsartefakten, die durch unterschiedliche Gewebeeigenschaften der Umgebung (Knochen, Gefäße, Luft) entstehen (Moessnang & Freiherr, 2013).

Es gibt Hinweise darauf, dass die neuronale Verarbeitung von Körpergerüchen sich von der anderer olfaktorischer Stimuli unterscheidet. So haben Lundström, Boyle, Zatorre und Jones-Gotman (2007) herausgefunden, dass zusätzlich zu den oben genannten Arealen, die für die Riecheindrücke verantwortlich sind, auch anteriorer und posteriorer cingulärer Kortex in Reaktion auf erwachsene Körpergerüche aktiviert werden. Bei der bisher kaum untersuchten Verarbeitung kindlicher Körpergerüche stellt sich die Frage, ob darüber hinaus noch weitere neuronale Strukturen beteiligt sind, um z. B. elterliches Annäherungsverhalten zu vermitteln.

Bisherige Befunde zu neuronaler Verarbeitung von Körpergerüchen in der Mutter-Kind-Beziehung

Aus der bildgebenden Forschung zu anderen Sinnesmodalitäten ist bekannt, dass elterliches Annäherungsverhalten mit spezifischen neuronalen Korrelaten einhergeht: Kringelbach et al. (2016) fassen in ihrer Übersichtsarbeit Studien bezüglich visueller und auditiver bindungsrelevanter Stimuli zusammen und arbeiten heraus, dass das erwachsene Gehirn in Reaktion auf solche Signale (z.B. Kindchenschema, Brabbeln) häufig Areale aktiviert, die Belohnung, Angenehmheit (pleasure) und daraus folgend Motivation zur Fürsorge vermitteln. Dazu zählen z. B. der anteriore cinguläre Cortex (ACC), die Insula, das ventrale Pallidum (VP) und Teile des OFC. Er schlägt ein übergeordnetes „Pleasure-Netzwerk“ vor, das in diesem Zusammenhang insbesondere kindliche Niedlichkeit (cuteness) neuronal kodiert und vermutet, dass dieses Netzwerk auf multimodale infantile Reize reagiert (Kringelbach et al., 2016).

Die neuronale Repräsentation bindungsspezifischer Chemosignale wurde bislang in zwei Studien überprüft: Lundström et al. (2013) verglichen Hirnaktivität in Reaktion auf Babygerüche mittels fMRT zwischen Müttern und Frauen, die keine Kinder hatten. Dabei wurde gezeigt, dass Babygerüche spezifische Belohnungsareale (Striatum) aktivieren und diese Aktivierungen bei den Müttern stärker ausgeprägt waren. Die Studie lieferte somit erstmalig Hinweise auf die affektive Bedeutsamkeit von Körpergerüchen auf neurobiologischer Ebene. Offen blieb hierbei jedoch, wie spezifisch die Aktivierungen sind, da nicht der Geruch des eigenen, sondern der eines unbekannten Babys präsentiert wurde; und ob sich Unterschiede zeigen, wenn Mütter tatsächlich das eigene Kind riechen. Eine ähnliche Untersuchung testete die mütterliche Wahrnehmung von Babygerüchen mittels funktioneller Nahinfrarotspektroskopie (fNIRS) und fand heraus, dass Mütter mit einer höheren Gesamtaktivität des Präfrontalkortex (PFC) auf Babygerüche reagieren als Frauen ohne Kinder (Nishitani, Kuwamoto, Takahira, Miyamura, & Shinohara, 2014). Diese Ergebnisse sind jedoch hinsichtlich der Funktionalität nicht präzise zu deuten, da durch fNIRS zwar generelle Aktivitätsänderungen abbildbar, aber keine spezifischen Lokalisierungen bezüglich einzelner Areale möglich sind.

Neuronale Verarbeitung von Körpergerüchen: Methodische Schwierigkeiten

Generell gibt es bisher nur wenige bildgebende Studien zur Wahrnehmung von Körpergerüchen, die heterogene Befunde zu neuronalen Korrelaten liefern. Diese sind schwierig zu vergleichen, da sie sowohl in der Methodenwahl als auch in den experimentellen Paradigmen stark variieren. Aktuell gibt es keine übereinstimmenden Konventionen darüber, wie man Körpergerüche, z. B. in einem fMRT-Design, optimal präsentiert. Schwierigkeiten, die sich bei solchen Studien ergeben, liegen zum einen in der Natur olfaktorischer Stimuli begründet, die konzentrationsabhängig sind (Moessnang & Freiherr, 2013). Die Konzentration bzw. Intensität von Körpergerüchen ist auf die Anzahl der

Moleküle pro Stoff, der den Körpergeruch enthält, limitiert. Weiterhin sind Körpergerüche aufwändig zu generieren und zu lagern. Zum anderen ist herausfordernd, dass Geruchsreize meist mit Hilfe stationärer Olfaktometer präsentiert werden. Auf diese Weise werden die Stimuli über einen kontinuierlichen Luftstrom computergestützt appliziert. Im MRT muss das Gerät oft außerhalb des Scanners platziert und mit langen Schläuchen mit dem Probanden verbunden werden, weshalb eine präzise Präsentation nicht einfach umzusetzen ist. Portable und atemgetriggerte Olfaktometer (Sezille et al., 2013; Sommer et al., 2012) können hier hilfreich sein, um den Weg zu verkürzen und eine genaue Reizpräsentation zu generieren. Darüber hinaus ist die Gewöhnung an Geruchsreize sowie die Länge der Stimulationsdauer zu berücksichtigen, die das neuronale Signal beeinflussen kann (Georgiopoulos et al., 2018; Moessnang & Freiherr, 2013).

Bedeutung kindlicher Körpergerüche für die Mutter-Kind-Beziehung: Veränderung im Laufe der Entwicklung

Beide oben genannte Studien zur neuronalen Repräsentation von Körpergerüchen im Rahmen der Mutter-Kind-Beziehung haben sich auf Babygerüche beschränkt; unklar ist jedoch, ob die mit Belohnung assoziierte affektive Bedeutsamkeit kindlicher Gerüche über die gesamte Entwicklungsspanne erhalten bleibt. Auch ist bisher nicht bekannt, ob die Fähigkeit, das eigene Kind am Geruch zu erkennen, über die gesamte Entwicklung des Kindes existiert oder ob dieser Mechanismus nur spezifisch für die Zeit unmittelbar nach der Geburt ausgelegt ist.

In diesem Zusammenhang berichtet eine Fragebogenstudie von einer kontinuierlichen Abnahme der Präferenz für den Geruch des eigenen Kindes im Laufe der Entwicklung (Croy, Frackowiak, Hummel, & Sorokowska, 2017). Bislang gibt es nur zwei Untersuchungen, die die elterliche Wahrnehmung kindlicher Körpergerüche bei älteren Kindern experimentell überprüft haben, und beide liefern heterogene Befunde. Weisfeld, Czilli, Phillips, Gall und Lichtmann (2003) testeten Bewertung und Identifikation von verwandten Körpergerüchen in insgesamt drei Studien. Die erste verdeutlichte, dass Erwachsene (N = 22) ihre Familienmitglieder am Geruch erkennen können, in der zweiten Studie wurde beobachtet, dass Mütter ihre biologischen Kinder, aber nicht ihre Stiefkinder, am Geruch erkennen können (N = 18), und die letzte Studie untersuchte familiäre Bewertungen des Körpergeruchs an insgesamt N = 17 Familien mit Kindern im Alter von 6-15 Jahren. Dabei zeigte sich, dass Mütter und Väter ihre Kinder am Geruch identifizieren können. Bezüglich der Präferenz unterschieden sich die Ergebnisse: Mütter bevorzugten den Geruch des fremden anstatt des eigenen Kindes. Väter präferierten den Geruch fremder Mädchen anstatt dem der eigenen Tochter, bei Söhnen war dies nicht der Fall. Umgekehrt zeigte sich ein ähnlicher Effekt: Pubertäre Mädchen bevorzugten den Geruch eines fremden

Erwachsenen vor dem des eigenen Vaters, dies traf beim mütterlichen Geruch hingegen nicht zu. Die Autoren interpretierten die Aversion gegenüber der pubertären Tochter bzw. dem Vater im Sinne negativen Imprintings, d.h., dass die olfaktorische Vermeidung der Inzuchtprävention im Sinne des Westermarck-Effekts dient. Der Westermarck-Effekt beschreibt sexuelles Desinteresse als Folge von Vertrautheit mit einer Person seit einer frühen Entwicklungsphase, in der sexuelles Verlangen nicht in Frage kam. Das Phänomen wurde erstmalig 1903 von Westermarck eingeführt (Westermarck, 1921) und als Ursachen wurden später olfaktorischen Mechanismen vermutet (Rantala & Marcinckowska, 2011; Schneider & Hendrix, 2000).

Ferdenzi, Schaal und Roberts (2010) zeigten in der zweiten Untersuchung an $N = 9$ Familien mit Kindern zwischen 7 und 18 Jahren, dass Mütter den Geruch ihres Kindes erkennen, Väter jedoch nicht. Bezüglich der Präferenz konnten sie den Westermarck-Effekt allerdings nicht replizieren, weshalb offen bleibt, ob negatives olfaktorisches Imprinting zwischen Eltern und Kindern tatsächlich existiert. Wenn existent, ist bisher unerforscht, wie eine solche Aversion biologisch vermittelt wird und welche Bestandteile des Körpergeruchs dazu beitragen.

Zusammensetzung von Körpergerüchen

Nach aktuellem Forschungsstand wird vermutet, dass Körpergerüche sich aus genetischen, entwicklungsbedingten (hormonellen) und umweltbedingten Komponenten zusammensetzen. Während genetische Einflüsse stabil sind, unterliegen die anderen Faktoren Schwankungen, die durch variable externe und entwicklungsabhängige Einflüsse bedingt sind (Havlíček, Fialová, & Roberts, 2017).

Stabile Faktoren: Genetik

Als genetischer Einflussfaktor wird auf Basis bisheriger Studien der hoch polymorphe Humane Leukozytantigenkomplex (HLA) beim Menschen bzw. Haupthistokompatibilitätskomplex (major histocompatibility complex, MHC) bei Tieren angeführt (Havlicek & Roberts, 2009). Dieser Komplex liegt auf dem kürzeren Telomer des sechsten Gens und ist für die körpereigene Immunabwehr verantwortlich, indem er pathogene Peptidfragemente an T- Zellen präsentiert, damit diese als fremd erkannt werden können. Innerhalb des Komplexes gibt es zwei Molekülklassen mit mehreren Genorten, auf denen je zwei Allelmerkmale ausgeprägt sind. Die erste Klasse (HLA-I) umfasst dabei die Loci HLA-A, -B, -C, –E, -F und -G; die Klasse HLA-II besteht aus den Loci HLA-DP, -DQ, und -DR (Fischer & Mayr, 2011).

Die Allele des jeweiligen Haplotyps werden einheitlich vererbt und jeder Genort setzt sich aus der Kombination eines väterlich sowie eines mütterlich vererbten Allels zusammen. Das

HLA-Profil spielt eine besondere Rolle in der Transplantationsmedizin, da es entscheidend für die Bestimmung der Histokompatibilität von Gewebe ist. Außerdem gibt es Zusammenhänge zwischen dem Auftreten bestimmter HL-Antigene und verschiedener Krankheiten (Fischer & Mayr, 2011). Gleichzeitig hat der HLA-Komplex auch im Rahmen der Geruchsforschung an Bedeutung gewonnen.

Aus Tierstudien ist bekannt, dass das MHC-Profil olfaktorisch wahrnehmbar ist und es die Paarung beeinflussen kann (Leinders-Zufall et al., 2004). Bei Mäusen und Fischen wurde beobachtet, dass diese die Paarung mit MHC-ähnlichen Partnern vermeiden. Dies impliziert zwei Vorteile: Zum einen erhöht es die Widerstandsfähigkeit der Nachkommen gegenüber Pathogenen, indem es MHC-Heterozygosität fördert. Zum anderen sorgt es dafür, dass Inzucht vermieden wird, was mit Vorteilen für die genetische Fitness der Nachkommen einher geht (Penn, 2002).

Auch beim Menschen scheinen HLA-Moleküle über die Riechfunktion detektierbar zu sein: So zeigen sich Unterschiede in der neuronalen Aktivität in Abhängigkeit von der genetischen Ähnlichkeit präsentierter synthetisierter HLA-Peptide (Milinski, Croy, Hummel, & Boehm, 2013). Auf Verhaltensebene konnten Wedekind, Seebeck, Bettens und Papeke 1995 erstmalig beobachten, dass Frauen männliche Körpergerüche positiver bewerteten, wenn diese zu ihrem eigenen HLA-Profil unähnlicher als wenn sie ähnlicher waren. Seither ist aufgrund von widersprüchlichen Ergebnissen nachfolgender Studien eine breite Debatte darüber entstanden, wie das HLA-Profil sich tatsächlich auf die menschliche Partnerwahl auswirkt (Havlicek & Roberts, 2009; Winternitz, Abbate, Huchard, Havlíček, & Garamszegi, 2017). Trotz vieler gegensätzlicher Untersuchungen konnten Wedekinds Befunde durch eine Studie unserer Arbeitsgruppe kürzlich teilweise repliziert werden (Sorokowska et al., 2018). Hier zeigte sich, dass Frauen Körpergerüche von Männern bevorzugen, die sich im HLA-Profil unterscheiden, spezifisch in den Allelen HLA-B und -C. Dies traf auf Frauen zu, die keine oralen Kontrazeptiva einnahmen. Frauen unter Einnahme oraler Kontrazeptiva und Männer verhielten sich anders – sie bevorzugten den Körpergeruch, der ihnen am vertrautesten war, unabhängig von der genetischen Ähnlichkeit. Jedoch ging es hier vor allem um die Wahrnehmung bzw. affektive Bewertung der Gerüche, nicht um die direkte Partnerwahl. Bei Betrachtung der tatsächlichen Wahl stellt sich dies anders dar: In einer weiteren Untersuchung unserer Arbeitsgruppe wurde die genetische Kompatibilität zwischen Ehepartnern an einer Stichprobe von N = 3760 deutschen verheirateten Paaren analysiert und ihre Ähnlichkeit mit dem Zufallslevel verglichen. Dabei zeigte sich, dass die Ehepaare sich tendenziell genetisch ähnlicher sind als per Zufall verteilt. Die Ergebnisse lassen sich durch verschiedene Ursachen erklären: Möglicherweise ist die Bedeutung rein biologischer Einflussfaktoren für eine Heiratsentscheidung sehr gering und wird von vielen weiteren Variablen, z. B. sozialem Status oder kulturellen Traditionen, überlagert (Dandine-Roulland,

Laurent, Dall'Ara, Toupance, & Chaix, 2019). Außerdem scheint die ethnische Gruppe eine Rolle zu spielen: Die Wahrscheinlichkeit, jemanden aus seiner eigenen ethnischen Gruppe zu heiraten, ist größer als jemanden aus einer fremden Gruppe; und die populationsspezifische Verteilung der Allelmerkmale führt bei Betrachtung der Gesamtbevölkerung dazu, dass häufig eine größere Ähnlichkeit innerhalb der Subgruppen entsteht.

Zusammengefasst lässt sich sagen, dass HLA-Komponenten über Geruch wahrnehmbar sind und sich auf die hedonische Bewertung des Körpergeruchs auswirken. Wie stark sich diese Bewertung in tatsächlichem Verhalten niederschlägt und wie dies insbesondere im Kontext der Eltern-Kind-Beziehung wirkt, bleibt offen. Forschungsarbeiten zu dieser Thematik haben den Einfluss genetischer Komponenten bisher außer Acht gelassen. Denkbar wäre, dass die genetische Ähnlichkeit im Sinne eines positiven olfaktorischen Imprintings zunächst die Identifikation sowie die Präferenz des Körpergeruchs des eigenen Kindes mediiert und auf diese Weise einen biologischen Mechanismus darstellt, der den Bindungsaufbau erleichtert. Verfolgt man diese Idee weiter, könnte es sein, dass sich der Effekt mit zunehmendem Alter umkehrt und Eltern ab der Pubertät ihres Kindes dessen Geruch als weniger angenehm empfinden und dafür genetisch unähnliche Gerüche bevorzugen. Dies könnte einen Mechanismus für den Westermarck-Effekt darstellen, bislang gibt es dazu jedoch noch keine Studien. Ebenso ist ungeklärt, wie groß der Varianzanteil dieser genetischen Faktoren an der gesamten Varianz, die die Wahrnehmung des Körpergeruchs ausmacht, ist.

Variable Faktoren: Umwelt

Weitere Komponenten, die Körpergerüche kennzeichnen, sind umweltbedingt. Hierzu zählen kulturspezifische Einflüsse und Ernährung; so konnte nachgewiesen werden, dass sich z. B. Fleischverzehr auf die Bewertung von Körpergerüchen niederschlägt (Havlíček et al., 2017). Außerdem werden Krankheitsstatus (Olsson et al., 2014), Gefühlszustände oder Persönlichkeitseigenschaften über Körpergerüchen transportiert (Lübke et al., 2014; Pause, Lübke, Laudien, & Ferstl, 2010; Prehn-Kristensen et al., 2009). All diese Faktoren können über verschiedene Zeiträume hinweg fluktuieren und sorgen daher für eine hohe Variabilität von Körpergerüchen sowie ihrer Wahrnehmung, weshalb es wichtig ist, solche Einflüsse im Hinblick auf mögliche Konfundierungen zu berücksichtigen.

Variable Faktoren: Hormone

Darüber hinaus gibt es Studien, die die Bedeutung entwicklungsbedingter bzw. hormoneller Bestandteile des Körpergeruchs herausstellen. Insbesondere zyklusabhängige Schwankungen im Körpergeruch sind gut dokumentiert: Generell werden weibliche Körpergerüche während der Ovulation angenehmer als in anderen Phasen bewertet (Singh

& Bronstad, 2001). Wie oben erwähnt ist außerdem bekannt, dass sich die Einnahme hormoneller Kontrazeptiva generell (Endevelt–Shapira et al., 2019) und in Interaktion mit genetischen Faktoren (Roberts, Gosling, Carter, & Petrie, 2008; Sorokowska et al., 2018) auf die Geruchswahrnehmung auswirkt.

Das hormonelle Profil ändert sich im Laufe der kindlichen Entwicklung: Zu Beginn der Pubertät gibt es einen deutlichen Anstieg der Steroidhormone, die zwar nicht direkt die Zusammensetzung des Körpergeruchs bestimmen, nach Transformation durch Hautbakterien jedoch über den Geruch wahrnehmbar werden (Kohl & Francoeur, 2002). Es wird vermutet, dass Steroidhormone eine Signalwirkung im Rahmen der Paarung bzw. Partnerwahl besitzen, da sie Informationen über die Gesundheit des Immunsystems liefern (Muehlenbein & Bribiescas, 2005). Estradiol und Testosteron sind in diesem Rahmen häufig untersuchte Steroide. Eine höhere Estradiolkonzentration steht z. B. im Zusammenhang mit erhöhter Attraktivität von weiblichen Gesichtern (Puts et al., 2013) und wirkt bei Mäusen auch auf olfaktorischer Ebene als Trigger für sexuelle Attraktivität (Ferkin & Johnston, 1993). Die Tatsache, dass weibliche Körpergerüche während der Ovulation am angenehmsten bewertet werden, spricht dafür, dass dieser bei Mäusen beobachtete Effekt auch bei Menschen zutrifft, denn während des Eisprungs ist die Estradiolkonzentration auf dem Höhepunkt (Nelson, 2000). Eine kürzlich veröffentlichte Studie bestätigt diese Hypothese und berichtet, dass die Bewertung weiblicher Körpergerüche positiv mit der gemessenen Estradiolkonzentration zusammenhängt (Lobmaier, Fischbacher, Wirthmüller, & Knoch, 2018), doch gibt es dazu noch keine weiteren Befunde. Hinsichtlich des Einflusses von Testosteron ist die Studienlage heterogen. Auch wenn einige Untersuchungen zeigen, dass die Testosteronkonzentration des Geruchsspenders mit einer intensiveren und negativeren Wahrnehmung des Körpergeruchs verknüpft ist (Doty, Orndorff, Leyden, & Kligman, 1978; Sergeant, 2010), widersprechen andere Studien diesem Befund (Rantala, Eriksson, Vainikka, & Kortet, 2006).

Körpergerüche als Hinweise auf den Entwicklungsstatus

Bislang gibt es keine Untersuchungen dazu, ob hormonbedingte Veränderungen im Körpergeruch auch im Langzeitverlauf abbildbar sind und auf dieser Ebene als Chemosignale zwischen Eltern und Kind wirken. Wie Kringelbach et al. (2016) vermuten, können infantile Signale eine universelle Niedlichkeit vermitteln, was sich auf elterliche Fürsorge im Sinne von Motivation und Annäherungsverhalten auswirkt. Es gibt Hinweise, dass eine solche auf neuronaler Ebene abbildbare Belohnung auch über den Körpergeruch eines Babys transportiert wird. Wenn außerdem auch entwicklungsbedingte Informationen, z. B. hormonelle Veränderungen, über den Körpergeruch gesendet werden, stellt sich die Frage, ob diese einen bestimmten Grad von körperlicher Reife vermitteln können. Auf diese

Weise könnten Körpergerüche je nach Entwicklungsstadium des Kindes auf die elterliche Wahrnehmung wirken und somit unterschiedliche Verhaltenstendenzen (Bindung vs. Ablösung) erleichtern.

4 Studienziele: Abgeleitete Forschungsfragen und Hypothesen

Bisherige Befunde verdeutlichen, dass Körpergerüchen als Chemosignale in der Eltern-Kind-Beziehung wirken und sowohl für die Identifikation des eigenen Kindes als auch für affektive Prozesse bedeutsam sind. Dennoch bleiben nach aktuellem Forschungsstand verschiedene Fragen offen, die im Rahmen der vorliegenden Doktorarbeit untersucht werden sollen.

Veröffentlichung 1: Body odours as a chemosignal in the mother-child relationship: new insights based on an human leucocyte antigen-genotyped family cohort

Hauptfragestellung: Mütter können ihre Kinder am Geruch erkennen und bevorzugen diesen Geruch gegenüber anderen Körpergerüchen. Unklar ist jedoch, ob dieser Effekt über die gesamte Entwicklungsspanne stabil bleibt und welche Rolle genetische und hormonelle Einflussfaktoren für die Wahrnehmung spielen.

Es wird die Hypothese aufgestellt, dass Mütter den Geruch des eigenen Kindes sowohl identifizieren (H1) als auch präferieren (H2) und beides bei HLA-ähnlichen Gerüchen stärker ausgeprägt ist als bei HLA-unähnlichen Gerüchen. Außerdem wird angenommen, dass die Präferenz für den Geruch des eigenen Kindes mit zunehmendem Alter geringer wird (H3), und dass Körpergerüche, die dem eigenen Kind zugeschrieben werden, positiver bewertet werden (H4). Es wird vermutet, dass Mütter den Körpergeruch des eigenen Sohnes mit Eintritt der Pubertät als weniger angenehm bewerten und dass dieser Effekt bei Töchtern nicht eintritt (H5).

Veröffentlichung 2: Children´s body odors: Hints to the development status

Hauptfragestellung: Es ist unklar, ob Körpergerüche den Entwicklungsstatus eines Kindes signalisieren können und ob dieser von Müttern detektiert wird.

Es wird die Hypothese aufgestellt, dass Mütter prä- und postpubertären Status von Kindern anhand von Körpergerüchen klassifizieren können (H1), und dass sie eine bessere Klassifikationsleistung zeigen, wenn sie mit dem jeweiligen Entwicklungsstadium vertraut sind (Bewertung von Körpergerüchen von Kindern, die gleichaltrig zum eigenen Kind sind; H2). Außerdem wird vermutet, dass sowohl die subjektive Bewertung des Geruchs (Angenehmheit, Intensität) als auch entwicklungsbedingte Informationen (pubertärer Status, Hormonkonzentration) diese Klassifikation beeinflussen (H3).

Veröffentlichung 3: The design matters: How to detect neural correlates of baby body odors

Hauptfragestellung: Bislang gibt es nur wenige und heterogene Befunde zur neuronalen Verarbeitung von Körpergerüchen und erst zwei Untersuchungen zu neuronalen Korrelaten kindlicher Körpergerüche im mütterlichen Gehirn. Bisherige Studien haben uneinheitliche Methoden verwendet, weshalb getestet werden soll, wie kindliche Körpergerüche mittels eines fMRT-Paradigmas optimal präsentiert werden können.

Es wird explorativ getestet, ob eine kurze, kontinuierliche Stimuluspräsentation besser geeignet ist als eine lange, gepulste Reizdarbietung, um neuronale Aktivität im mütterlichen Gehirn in Reaktion auf Babygerüche abzubilden (H1).

Nachfolgend soll diese Studie als Grundlage für die Untersuchung der neurobiologischen Verarbeitung von Babygerüchen im mütterlichen Gehirn dienen, bei der die neuronale Aktivität zwischen der Reaktion auf den Körpergeruch des eigenen und eines fremden Babys verglichen wird. Darüber hinaus soll überprüft werden, ob der kindliche Körpergeruch als Niedlichkeitsreiz verarbeitet wird, indem die neuronale Aktivität spezifisch in belohnungsbezogenen Arealen sowie den Strukturen des Pleasure-Netzwerks (Kringelbach et al., 2016) betrachtet wird. Dieser Teil der Arbeit ist jedoch noch nicht publiziert und wird daher nur kurz im Anschluss an die hier berichteten Ergebnisse vorgestellt und diskutiert.

5 Methodik der Untersuchungen

Der folgende Abschnitt liefert einen Überblick über die verwendete Untersuchungsmethodik. Weitere Details sind den Veröffentlichungen 1-3 zu entnehmen.

Alle hier vorgestellten Untersuchungen fanden im Rahmen des DFG-Projekts (CR479/4-1) “The impact of body odor on bonding and incest avoidance over the course of life: A developmental and neuropsychological approach” statt. Die Ethikkommission der TU Dresden genehmigte die Durchführung der Studien (Ethikvotum EK 104032015). Alle Teilnehmenden wurden vorab über das Studienvorhaben aufgeklärt und erklärten schriftlich ihre Einwilligung zur Studienteilnahme.

Stichprobenbeschreibung und Studienablauf

Insgesamt wurden bis zum Oktober 2019 N = 300 Familien für das gesamte Projekt rekrutiert, darunter auch Väter. Da die Stichprobe der Väter jedoch nicht ausreichend für einen statistischen Vergleich war (N = 59), wurden nur die Mütter in die vorliegenden Arbeiten einbezogen.

Für die Veröffentlichungen 1 und 2 wurde dieselbe Stichprobe verwendet. Diese bestand aus insgesamt *N* = 164 Müttern (*MW* = 37.5 ± 7.8 Jahre) mit *N* = 226 Kinder (102 Jungen, 104 Mädchen, Alter: *MW* = 7.6 ± 5.9 Jahre). Für Veröffentlichung 3 wurden *N* = 10 Mütter (*MW* = 32.2 ± 4.7 Jahre) mit Kindern unter zwei Jahren (*MW* = 10.30 ± = 4.22 Monate) aus der bestehenden Stichprobe rekrutiert. Diese Untersuchung diente als Pilotstudie für die weiterführende fMRT-Studie, die von Mai – Juni 2018 mit *N* = 38 Müttern (*MW* = 32.1 ± 3.1 Jahre) durchgeführt wurde. Darauf basierend fand im Oktober 2019 eine nachfolgende fMRT-Untersuchung mit *N* = 60 Probanden (*n* = 20 Mütter, *n* = 20 Frauen ohne Kinder, *n* = 20 Väter) statt, die zur Zeit noch ausgewertet und daher nicht in dieser Arbeit berücksichtigt wird.

Die teilnehmenden Familien wurden zu einem ersten Untersuchungstermin in der Klinik und Poliklinik für Psychotherapie und Psychosomatik des Universitätsklinikums Dresden eingeladen, bei dem die Aufklärung über den Studienablauf sowie die Überprüfung der Einschluss- (biologische Mutterschaft, normosmisches Riechvermögen) und Ausschlusskriterien (aktuelle Schwangerschaft der Mutter, unzureichende Deutschkenntnisse) erfolgte. Im Anschluss wurden Wangenabstriche für die genetische Analyse entnommen und die Familien bekamen ein Studienset ausgehändigt, das alle Utensilien für die Gewinnung der Körpergeruchsproben sowie die Entnahme der Speichelproben enthielt (s. Veröffentlichung 1). Zusätzlich wurden die Eltern gebeten, anamnestische Angaben zu medizinischen und soziodemografischen Variablen über sich selbst und das Kind sowie zur Eltern-Kind-Beziehung zu machen. Letzteres beinhaltete die Einschätzung der Qualität und Nähe der Beziehung zum Kind auf einer 5-stufigen Likertskala von 1 „gar nicht“ bis 5 „sehr“, sowie Angaben dazu, wie viele Stunden pro Tag mit dem Kind verbracht werden und wie viel Prozent der Erziehung übernommen wird. Außerdem sollten die Eltern standardisierte Fragebögen zur Bindungsqualität (Postpartum Bonding Questionnaire, PBQ, (Brockington, Fraser, & Wilson, 2006)), zur Belohnungssensitivität (Behavioral Inhibition System Behavioral Activation System Scales, BisBas, (Strobel, Beauducel, Debener, & Brocke, 2001)) sowie zur Depressivität (Beck Depressions Inventar II, BDI II, (Hautzinger, Keller, & Kühner, 2006)) ausfüllen. Die ersten beiden Fragebögen dienten dazu, Kontrollvariablen zu generieren, die im Zusammenhang mit der Wahrnehmung des Körpergeruchs stehen können. Für die Bindungsqualität zeigte eine vorhergehende Studie, dass Mütter mit Bindungsstörungen den Geruch des eigenen Kindes schlechter identifizieren können und als weniger belohnend empfinden als gesunde Mütter (Croy et al., 2019). Die Belohnungssensitivität wurde erhoben, um zu explorieren, ob diese im Zusammenhang mit der neuronalen Verarbeitung der Körpergerüche steht und Mütter mit erhöhter Belohnungssensitivität auch den Körpergeruch dementsprechend als belohnender empfinden. Der Fragebogen zur Depressivität diente als Screening auf psychopathologische

Symptomatik, außerdem gibt es Hinweise auf Assoziationen zwischen Depressivität und Riechvermögen (Croy & Hummel, 2017), weshalb ein solcher Einfluss ebenfalls überprüft werden sollte.

Genetische Analyse: Bestimmung des HLA-Profils

Die Analyse der genetischen Proben erfolgte mittels next-generation sequencing (Lange et al., 2014; Schöfl et al., 2017) anhand von hochaufgelöster Typisierung und Bestimmung der Nukleotidsequenz der Exone 2 und 3 von HLA-A, -B, -C, -DRB1, -DQB1 und –DPB1 durch das ASHI(American Society for Histocompatibility and Immunogenetics)-akkreditierte Labor DKMS Life Science Lab in Dresden.

Im Rahmen der Veröffentlichung 1 wurde die genetische Ähnlichkeit für die Zuordnung von HLA-ähnlichen und –unähnlichen Proben zum mütterlichen HLA-Profil wie folgt festgelegt: Eine Übereinstimmung von mindestens einem Allel in den Genorten HLA-B und/oder –C (Kromer et al., 2016; Sorokowska et al., 2018) wurde als HLA-Ähnlichkeit definiert. Keine Übereinstimmungen in diesen Allelen wurden als HLA-Unähnlichkeit definiert.

Gewinnung der Körpergeruchsproben

Für die Gewinnung der Körpergerüche sollten die Kinder nach standardisiertem Protokoll (s. Veröffentlichung 1) eine Nacht in einem von uns zur Verfügung gestellten T-Shirt bzw. Body in der jeweiligen Größe des Kindes schlafen. Nach der Testnacht sollte das Kleidungsstück in einem Zip-Beutel verpackt und unmittelbar zurück ins Labor gebracht werden bzw. wurde von der Versuchsleiterin eingesammelt, wenn dies nicht möglich war. Im Labor wurden die Proben bis zur Testung bei -25°C eingefroren.

Bestimmung des Entwicklungsstatus

Bei allen Kindern ab dem Alter von fünf Jahren wurde der Entwicklungsstatus durch zwei Variablen bestimmt:

1. Steroidhormonstatus: Mit Hilfe einer Salivette☕ (code blue, SARSTEDT AG & Co. KG, Nümbrecht, Germany) wurde eine Speichelprobe zur Bestimmung der Hormonkonzentration der Steroidhormone Estradiol und Testosteron entnommen. Dies sollte am Abend vor der Testnacht geschehen, damit das Hormonlevel in direktem Zusammenhang zur Körpergeruchsprobe abgebildet werden konnte. Die Salivette wurde über Nacht im Kühlschrank gelagert, am nächsten Morgen gemeinsam mit den Körpergeruchsproben abgegeben und anschließend im Labor bei -25°C bis zur Analyse eingefroren. Dafür wurde die Testosteron- und Estradiolkonzentration für jede Probe mittels Immuno-Assay analysiert (Dresden Lab Service GmbH).

2. Pubertärer Status: Zusätzlich sollten die Mütter den pubertären Status des Kindes anhand des Vorliegens sekundärer Geschlechtsmerkmale durch die Pubertal Development Scale (PDS, (Watzlawik, 2009)) einschätzen (s. Veröffentlichungen 1 und 2).

Testung: Mütterliche Geruchsbewertung

Nach Probenerhalt und Bestimmung des HLA-Profils wurden die Mütter zur Testung eingeladen, bei der sie in einer standardisierten Prozedur sechs Körpergeruchsproben bewerten, die sich wie folgt zusammensetzten: a) eigenes Kind; b) HLA-ähnliches Kind, gleiche Altersgruppe; c) HLA-unähnliches Kind, gleiche Altersgruppe; d) HLA- ähnliches Kind, andere Altersgruppe; e) HLA-unähnliches Kind, andere Altersgruppe; f) neutrale Geruchsprobe (ungetragenes T-Shirt), die zur Kontrolle der Intensität der Stimuli diente.

Die beiden Proben d) und e) wurden so ausgewählt, dass sie möglichst einen anderen Entwicklungsstatus als den des eigenen Kindes abbildeten. Pro Durchgang bewerteten die Mütter eine der folgenden Dimensionen auf visuellen Analogskalen von 0 („gar nicht“) bis 100 („sehr“): Angenehmheit, Intensität, Wanting („Wie sehr möchte ich den Geruch noch einmal riechen“), Süßlichkeit, Attraktivität des Geruchs. Zusätzlich wurden sie gebeten, die Altersgruppe des Spenders der jeweiligen Geruchsprobe einzuschätzen und konnten dabei aus sechs Kategorien wählen: 0-1 Jahr, 1-3 Jahre, 4-8 Jahre, 9-13 und 14-18 Jahre. Zuletzt sollten die Mütter den Geruch des eigenen Kindes aus allen dargebotenen Proben identifizieren.

fMRT-Studie

Die für die fMRT-Studie rekrutierten Mütter nahmen ebenso an der oben beschriebenen Prozedur teil. Ferner kamen sie zu einer 45-minütigen MRT-Sitzung, in welcher die Körpergeruchsprobe des eigenen und eines altersgematchten unbekannten Babys in insgesamt vier funktionellen T2*-gewichteten Messungen (TR = 2.5 Sekunden, TE 51 Millisekunden) mittels zwei verschiedener Paradigmen randomisiert dargeboten wurde. Das erste Paradigma war ein langes Blockdesign, welches acht Geruchspräsentationen á 15 Sekunden beinhaltete, in denen der Körpergeruch gepulst dargeboten wurde (1 Sekunde Geruch alternierend mit 2 Sekunden Luft), gefolgt von einem Block von 30 Sekunden ohne Geruchsdarbietung (Baselinebedingung). Das zweite Paradigma war durch eine kurze, aber kontinuierliche Stimuluspräsentation gekennzeichnet (13 Blöcke á 6 Sekunden durchgehende Geruchspräsentation, jeweils gefolgt von einem Block á 19 Sekunden ohne Geruchsdarbietung). Die Unterschiede dienten dazu, den Einfluss von Dauer, Art und Anzahl der Wiederholungen pro Stimulusdarbietung zu ermitteln und hinsichtlich der neuronalen Reaktionen vergleichen zu können. Außerdem erfolgte eine hochaufgelöste strukturelle Messung des Gehirns (T1 Sequenz, TR = 2.5 Sekunden), um die funktionellen Bilder später

anatomisch präzise zuzuordnen. Die Daten wurden mit einem Siemens 3T Scanner (SONATA, 8-Kanal Kopfspule) aufgenommen (s. Veröffentlichung 3).

Statistische Auswertung

Die statistische Analyse der Daten wurde mit IBM SPSS Statistics 25 (IBM Corp. Released 2017, IBM SPSS Statistics für Windows, Version 25.0, Armonk, NY: IBM Corp) durchgeführt. Die Auswertung der fMRT-Daten erfolgte mit SPM12 (Wellcome Trust Center for Neuroimaging, London, UK, implementiert in Matlab R2014b MathWorks, Inc., Natick, MA, USA) sowie mit der MarsBar-Toolbox (Brett, Anton, Valabregue, & Poline, 2002).

6 Zusammenfassung der Ergebnisse

Die oben dargestellten Studien bestätigen, dass Körpergerüche als bedeutsame Chemosignale in der Mutter-Kind-Beziehung wirken. Sie können sowohl die Identifikation, als auch eine affektive Bevorzugung des eigenen Kindes vermitteln (Veröffentlichung 1) und Informationen über den Entwicklungsstatus transportieren (Veröffentlichung 2). Um neuronale Aktivität in Reaktion auf kindliche Gerüche abzubilden, empfiehlt sich eine kurze, kontinuierliche Stimuluspräsentation (Veröffentlichung 3).

Veröffentlichung 1: Body odours as a chemosignal in the mother-child relationship: new insights based on an human leucocyte antigen-genotyped family cohort

H1 konnte teilweise bestätigt werden: Die Mütter erkannten ihr eigenes Kind überzufällig häufig am Geruch, dies stand jedoch nicht im Zusammenhang mit der HLA-Ähnlichkeit. Bei spezifischem Vergleich der Altersgruppen wurde deutlich, dass die Identifikationsleistung in der frühen Pubertät (9-13 Jahre) auf Zufallslevel sank.

Im Einklang mit H2 zeigte sich eine Bevorzugung des Körpergeruchs des eigenen Kindes gegenüber allen unbekannten Körpergerüchen. Der zweitangenehmste Geruch war der des gleichaltrigen und HLA-ähnlichen Kindes, das sich im paarweisen Vergleich nicht signifikant von dem des eigenen Kindes unterschied.

Für H3 konnte kein globaler Alterseffekt beobachtet werden, bei einzelner Analyse der Altersgruppen zeigte sich allerdings eine Ausnahme für die Phase der frühen Pubertät (9-13 Jahre): In diesem Zeitraum wurde der Geruch des eigenen Kindes nicht gegenüber fremden Körpergerüchen präferiert.

Wie zuvor erwartet, hing das Identifikationsverhalten mit der impliziten Präferenz eines Geruchs zusammen (H4): Über alle Altersgruppen hinweg wurden jene Körpergerüche, die

als vom eigenen Kind stammend ausgewählt wurden, angenehmer bewertet als die nicht ausgewählten Gerüche, unabhängig davon, ob die Zuordnung falsch oder korrekt war.

H5 konnte für die Phase der frühen Pubertät bestätigt werden, in der eine negative Beziehung zwischen dem Testosteronspiegel und der Angenehmheit des Geruchs beobachtet wurde: Der Körpergeruch des eigenen Sohns (9-13 Jahre) wurde bei höherem Testosteronspiegel des Sohns unangenehmer bewertet, dies war bei der Geruchsbewertung gleichaltriger unbekannten Jungen nicht der Fall. Bei Töchtern in dieser Altersgruppe zeigte sich eine Tendenz der Mütter, den Geruch mit steigendem Estradiolspiegel als angenehmer zu bewerten, dieser Zusammenhang war jedoch nicht signifikant.

Interessant ist, dass die Bewertung des eigenen Sohns in der postpubertären Phase (14-18 Jahre) der Bewertung präpubertärer Kinder ähnelte. In dieser Altersgruppe konnten die Mütter das eigene Kind wieder am Geruch identifizieren und präferierten den Körpergeruch im Vergleich zu fremden Kindern. Dies deutet darauf hin, dass die Vertrautheit mit dem Körpergeruch einen entscheidenden Einfluss auf dessen Bewertung hat; und diese Vertrautheit im Zeitraum der frühen Pubertät aufgrund des Steroidhormonanstiegs und den dadurch bedingten Veränderungen im Körpergeruch kurzzeitig verloren geht.

Veröffentlichung 2: Children´s body odors: Hints to the development status

Bezüglich H1 zeigte sich, dass Mütter den Entwicklungsstatus des Kindes mit einer Genauigkeit von 64 % korrekt klassifizieren können. Außerdem tendierten die Mütter dazu, kindliche Körpergerüche als präpubertär zu bewerten.

Für H2 bestätigte sich, dass die Mütter besser in der Klassifikation abschneiden, wenn die zugehörige Probe aus der gleichen Altersklasse wie das eigene Kind stammt.

Wie in H3 angenommen, basierten die Mütter die entwicklungsspezifische Klassifikation des Körpergeruchs auf ihrem perzeptuellen Eindruck (Angenehmheit, Intensität) sowie auf der Beurteilung sekundärer Geschlechtsmerkmale (Einschätzung des pubertären Status). Letzteres traf nur für die Mütter zu, welche Kinder im postpubertären Alter hatten. Unabhängig vom Alter des eigenen Kindes konnte bei allen Müttern beobachtet werden, dass eine höhere Angenehmheitsbewertung mit der Klassifizierung eines Geruchs als präpubertär zusammenhing, während eine höhere Intensitätswahrnehmung zur postpubertären Klassifizierung eines Körpergeruchs führte. Entgegen der Vermutung zeigte sich kein Einfluss der Steroidhormonkonzentration auf die mütterliche Klassifikation.

Veröffentlichung 3: The design matters: How to detect neural correlates of baby body odors

Der Vergleich der neuronalen Aktivität in Reaktion auf eine kurze, kontinuierliche vs. eine längere, gepulste Reizdarbietung zeigte insgesamt stärkere Aktivierungen nach der kurzen Stimuluspräsentation (H1). Dies wurde anhand der neuronalen Aktivität verschiedener vorher definierter Regionen (Regions of Interest, ROIs) beobachtet, die aus bisherigen Studien bekannte Areale zur Riech- und Körpergeruchsverarbeitung umfassten. Trotz der allgemeinen Überlegenheit der kurzen Reizpräsentation, zeigte der systematische Vergleich der Faktoren (Anzahl der Wiederholungen, Dauer und Art der Stimulation) differentielle Effekte auf die jeweiligen ROIs. Während die Amygdala als Teil des primären olfaktorischen Kortexes deutlich von dem kurzen Design (kurze Stimulation, kontinuierliche Präsentation, weniger Wiederholungen pro Durchgang) profitierte, reagierte der OFC als sekundäre Riechstruktur mit stärkerer neuronalen Aktivität auf das lange Design (lange Stimulation, viele Wiederholungen pro Durchgang).

7 Diskussion und Ausblick

Einordnung der Ergebnisse

Betrachtet man die hier angeführten Ergebnisse im Kontext des aktuellen Forschungsstandes, zeigt sich, dass bisherige Befunde aus experimentellen Studien hinsichtlich der Identifikation sowie der Präferenz des Körpergeruchs des eigenen Kindes (Croy et al., 2019; Ferdenzi et al., 2010; Porter et al., 1983; Weisfeld, Czilli, Phillips, Gall, & Lichtman, 2003) zum Teil repliziert werden konnten: Die Mütter waren in der Lage den Geruch des eigenen Kindes zu erkennen und bevorzugten diesen im Vergleich zu Körpergerüchen fremder Kinder. Dies galt für alle Entwicklungsstadien, bis auf die Phase der frühen Pubertät. Ursachen für die veränderte Wahrnehmung während dieser Zeit liegen möglicherweise in der reduzierten Vertrautheit des Geruchs. In der initialen Pubertät führt der Anstieg der Steroidhormone (Dorn, Dahl, Woodward, & Biro, 2006) vermutlich zu einer veränderten Wirkung des Körpergeruchs, der die Wahrnehmung der Mütter irritiert, weshalb der Geruch als weniger angenehm bewertet wird. Mit zunehmendem Entwicklungsstatus scheint es so, als ob die Mütter sich wieder an den Geruch gewöhnen, und dieser, sobald erneut als vertraut wahrgenommen, auch erkannt und bevorzugt wird (Delplanque et al., 2008).

Die im Rahmen dieser Doktorarbeit durchgeführte Studie unterschied sich von vorhergehenden Untersuchungen zunächst aufgrund der weitaus größeren Stichprobenanzahl (hier: N = 164 vs. Ferdenzi et al., 2010: N = 9; Weisfeld et al., 2003: N = 17; Porter et al., 1983: N = 20; Croy et al., 2019: N = 50) sowie der umfassenden Altersspanne, die untersucht wurde (hier: 0-18 Jahre; Ferdenzi et al., 2010: 7-18 Jahre; Weisfeld et al., 2003: 6-15 Jahre, Porter et al., 1983: 7-41 Stunden postpartum, Croy et al., 2019: 0-1 Jahr). Darüber hinaus wurden in dieser Arbeit erstmalig die Einflüsse von Genetik (HLA-Profil) sowie hormonellem Status systematisch überprüft.

Die vorangestellten Hypothesen hinsichtlich der Auswirkungen der HLA-Ähnlichkeit auf die Körpergeruchswahrnehmung ließen sich nur bezüglich der Präferenz, nicht jedoch für die Identifikation bestätigen. Dies kann daran liegen, dass die genetische Komponente zwar zur Identifikation eines Geruchs als vertraut beiträgt, Vertrautheit sich allerdings noch aus weiteren Komponenten zusammensetzt, die über den genetischen Einfluss hinaus reichen. Entsprechendes wurde bei Fischen (Griffiths & Magurran, 1999; Ward & Hart, 2003) und Schimpansen beobachtet (Goodall, 1986), trifft aber auch auf Menschen zu: So dienen nicht nur das gemeinsame Aufwachsen (Bevc & Silverman, 2000), sondern auch Faktoren, wie z. B. das Beobachten einer dauerhaften Interaktion zwischen einem anderen Individuum und der eigenen Mutter (Lieberman, Tooby, & Cosmides, 2007; Park, Schaller, & Van Vugt, 2008) als Hinweisreize, um Verwandtschaft, in diesem Fall Geschwister, zu erkennen.

Abgesehen davon ist die Erfassung des HLA-Profils komplex. Für die vorliegende Auswertung wurde sich auf die zuvor festgelegten Loci HLA-B und -C Allele der Klasse I beschränkt, da für diese bekannt ist, dass sie die Körpergeruchswahrnehmung beeinflussen (Kromer et al., 2016; Sorokowska et al., 2018). Mittels explorativer Datenanalysen wurde zusätzlich der Einfluss jedes Loci einzeln sowie in Kombination betrachtet und eine im Rahmen einer weiterführenden Studie entwickelte Auswertungsmethode angewendet. Die genetische Passung lässt sich demnach nicht nur über gleiche bzw. verschiedene Allelkombinationen (HLA-Ähnlichkeit bzw. -Unähnlichkeit) abbilden, sondern auch über den erwarteten Wert, dass aus einer Kombination der verschiedenen Allelprofile homozygote Nachkommen entstehen. Bei diesem Ansatz wird vor allem der evolutionäre Vorteil der Paarung mit kompatiblen Partnern betrachtet, der die Vielfalt im Immunsystem der Nachkommen erhöhen kann. Diese Auswertungsmethode zeigte allerdings keinen Einfluss auf die mütterliche Geruchsbewertung und wurde aufgrund der Übersichtlichkeit aus der Darstellung dieser Arbeit weggelassen (s. Supplementary Material, Veröffentlichung 1). Überdies bleibt offen, ob noch weitere genetische Merkmale außer dem HLA-Profil den Körpergeruch prägen. Eine kürzlich veröffentlichte genomweite Analyse zeigt in diesem Zusammenhang, dass Hinweise auf assortative bzw. dissortative Paarung innerhalb des ganzen Genoms zu finden sind und sich nicht spezifisch für die HLA-Region unterscheiden (Nishi, Alexander, Fowler, & Christakis, 2020).

Ähnliches ist bezüglich der Befunde zu hormonellen Einflüssen zu berücksichtigen. Auch wenn die Steroidhormonkonzentration mit der hedonischen Wahrnehmung assoziiert ist, scheint sie nicht unmittelbar an der Klassifizierung des Entwicklungsstadiums beteiligt zu sein. Der Pubertätsbeginn ist durch eine Kaskade verschiedener hormoneller Prozesse gekennzeichnet (Grumbach, 2002), die in der aktuellen Arbeit nicht betrachtet wurden. Testosteron und Estradiol sind zwar geeignet, um die hormonelle Entwicklung der Pubertät abzubilden (Dorn et al., 2006), diese korreliert jedoch nicht zuverlässig mit der physischen Entwicklung (Shirtcliff, Dahl, & Pollak, 2009). Außerdem ist zu berücksichtigen, dass Steroidhormone Tagesschwankungen unterliegen (Landman, Sanford, Howland, Dawes, & Pritchard, 1976). Durch die Instruktion der Probanden, die Speichelproben immer am Abend vor der Testnacht zu entnehmen, wurde versucht, eine direkte Assoziation zwischen Hormonlevel und Körpergeruch herzustellen. In zukünftige Messungen sollte jedoch auch der morgendliche hormonelle Status erhoben werden, um Fluktuationen im Zusammenhang mit Körpergeruch präziser abzubilden.

Mutter-Kind-Bindung: Limitationen und Ausblick

Im Hinblick auf die Eltern-Kind-Beziehung stellt sich die Frage nach den Implikationen der vorgestellten Ergebnisse für die Qualität der Interaktion bzw. für das elterliche Verhalten

gegenüber dem Kind. Die hier erfassten Unterschiede in der Beziehungsqualität zeigten keinen Einfluss auf die Ergebnisse. Das mag daran liegen, dass die Fragen zu Beziehung- und Bindungsqualität dahingehend limitiert sind, dass sie die Varianz einer gesunden Stichprobe nicht ausreichend abbilden. Die Mutter-Kind-Beziehung wurde im Rahmen dieser Doktorarbeit nur als Kontrollvariable einbezogen, um mögliche konfundierende Einflüsse auf die Ergebnisse zu berücksichtigen (Croy et al., 2019), jedoch nicht, um die Bindungsqualität präzise zu erheben. Das hier verwendete Instrument zur Erfassung der postpartalen Bindung wird zur Diagnostik psychischer Störungen eingesetzt (Brockington et al., 2006) und ist daher ungeeignet, um subtile Differenzen in einer gesunden Stichprobe zu detektieren. In weiterführenden Studien, die sich auf die Bedeutung der Geruchswahrnehmung für die tatsächliche Interaktion zwischen Eltern und Kind beziehen, sollte dies berücksichtig werden. Bindung könnte zum einen durch umfassendere Fragebögen (z. B. Multiperspektivischer Fragebogen zur Eltern-Kind-Beziehung, MEK, (Müller & Achtergarde, 2018)) sowie zum anderen durch die Videoaufnahme kurzer Interaktionssequenzen erfasst werden, welche sich als valide in der Bindungsforschung erwiesen haben (Lotzin et al., 2015).

Eine vorhergehende Arbeit von Dubas et al. (2009) zeigte, dass Väter mit bestrafenderem Erziehungsverhalten auch schlechter in der Geruchsidentifikation abschnitten, dies war bei Müttern nicht der Fall. In ihrer Studie wurden jedoch nur Kinder im Alter von 8-9 Jahren eingeschlossen und es bleibt unklar, ob ein solcher Zusammenhang auch in anderen Entwicklungsstufen existiert. Die dort untersuchte Altersgruppe (8-9 Jahre) markiert den Übergang zur gonadalen Phase, welche durch einen Steroidhormonanstieg gekennzeichnet ist (Dorn et al., 2006). In Anbetracht der Ergebnisse aus Veröffentlichung 1 sollte in zukünftigen Untersuchungen mit Fokus auf dem Erziehungsstil daher auch der pubertäre bzw. hormonelle Status berücksichtigt werden, um mögliche Konfundierungen auszuschließen.

Neuronale Korrelate von Babygerüchen

Die Tendenz der Mütter, die präsentierten Gerüche als präpubertär zu klassifizieren, unterstützt die Annahme, dass Körpergerüche von Kindern eine inhärente affektive Bedeutsamkeit transportieren, die die mütterliche Bindung an das Kind erleichtert. Damit einhergehend berichten Okamoto et al. (2016), dass Eltern den kindlichen Geruch insbesondere in den ersten Lebensjahren als Quelle affektiver Zuneigung zum Kind nutzen. Diese Bedeutsamkeit olfaktorischer Signale für die Zuneigung zum eigenen Kind entspricht dem von Kringelbach et al. (2016) vorgestellten Modell der Niedlichkeit, welche durch multimodale kindliche Reize ausgelöst wird und, wie für visuelle und auditive Stimuli gezeigt, auf neurobiologischer Ebene Belohnung und Angenehmheit vermittelt. Um dies auch für chemosensorische Stimuli zu überprüfen, wurde die hier präsentierte Studie zur neuronalen

Wahrnehmung von Körpergerüchen (Veröffentlichung 3) durchgeführt, damit zunächst ein bestmögliches Paradigma für die Darbietung von Babygerüchen entwickelt werden konnte. Die Unterschiede in der neuronalen Aktivität zwischen dem Ansprechen der einzelnen Regionen auf die verschiedenen Paradigmen sind vermutlich durch spezifische Charakteristika der jeweiligen Strukturen bedingt: Zum einen gibt es Befunde dazu, dass primäre Riechstrukturen schnell an Gerüche habituieren und adaptieren (Poellinger et al., 2001), weshalb eine höhere Frequenz an Durchgängen mit jeweils wenigen, kurzen Reizdarbietungen empfehlenswert ist, um eine ausreichende Darbietungsstärke zu erhalten. Das BOLD(blood oxygenation level dependence)-Signal unterscheidet sich im Zeitverlauf zwischen primären Riecharealen und dem sekundär nachgeschalteten OFC – diese Region braucht länger, um auf eine olfaktorische Stimulation anzusprechen, was möglicherweise mit der zusätzlichen Verschaltung über den Thalamus zusammenhängt (Poellinger et al., 2001). Die in Veröffentlichung 3 gewonnenen Erkenntnisse verdeutlichen, dass unter Berücksichtigung des spezifischen Interesses an bestimmten Hirnstrukturen zwischen Dauer der Stimulation, Gesamtdauer des Experiments und Wiederholungen abgewogen und dementsprechend andere Schwerpunkte im Design gesetzt werden müssen. Das kurze Design lässt sich jedoch empfehlen, um insgesamt robuste Aktivierungen zu erhalten, weshalb dieses auch in den nachfolgenden fMRT-Studien verwendet wurde, die im Rahmen dieses Projekts durchgeführt wurden.

Olfaktorisches Kindchenschema?

Die erste auf diesem Design basierende Studie, die im Rahmen dieser Dissertationsphase zwar noch nicht publiziert, aber abgeschlossen und ausgewertet wurde, untersuchte neuronale Korrelate von Babygerüchen im mütterlichen Gehirn. Dafür wurden N = 38 gesunden Müttern der Geruch des eigenen und eines alters- und geschlechtsgematchten fremden Babys präsentiert (je zweimal in randomisierter Reihenfolge, s. Abbildung 1A), um den globalen Effekt des Babygeruchs (vs. Kontrollbedingung (Luft)) sowie den spezifischen Effekt des Geruchs des eigenen Babys auf die neuronale Aktivität zu untersuchen. Die Studie liefert Evidenz dafür, dass infantile Chemosignale ebenso wie Reize aus anderen Modalitäten auf neurobiologischer Ebene Niedlichkeit und Belohnung vermitteln. Im Detail zeigen die Ergebnisse, dass Babygerüche neuronale Aktivität im mütterlichen Gehirn sowohl in Belohnungsarealen als auch im Pleasure-Netzwerk auslösen (Schäfer, Michael, & Croy, 2019). Eine nachfolgende Konnektivitätsanalyse konnte darüber hinaus belegen, dass die Aktivierung in den jeweiligen Arealen des Pleasure-Netzwerks auch untereinander positiv miteinander korrelieren (s. Abbildung 1C, (Kressner-Kiel, 2019)). Die durch den Fragebogen erhobene Belohnungssensitivität hatte keinen Einfluss auf die Stärke der neuronalen Aktivität. Auffallend war, dass die implizite Präferenz für den Geruch des eigenen Kindes, wie sie in der Verhaltensstudie (Veröffentlichung 1) erfasst wurde, mittels fMRT nicht

beobachtbar war, da sich die neuronale Aktivität als Reaktion auf den Geruch des eigenen im Vergleich zu einem unbekannten Baby nicht unterschied (Schäfer et al., 2019). Daraus lässt sich die Hypothese ableiten, dass der Babygeruch, ähnlich wie das Kindchenschema, als universeller Stimulus wirkt, der unabhängig von elterlichem Status Motivation zur Fürsorge auslöst (Glocker et al., 2009). Dies widerspricht bisherigen Befunden zur Verarbeitung von Babygerüchen zunächst:

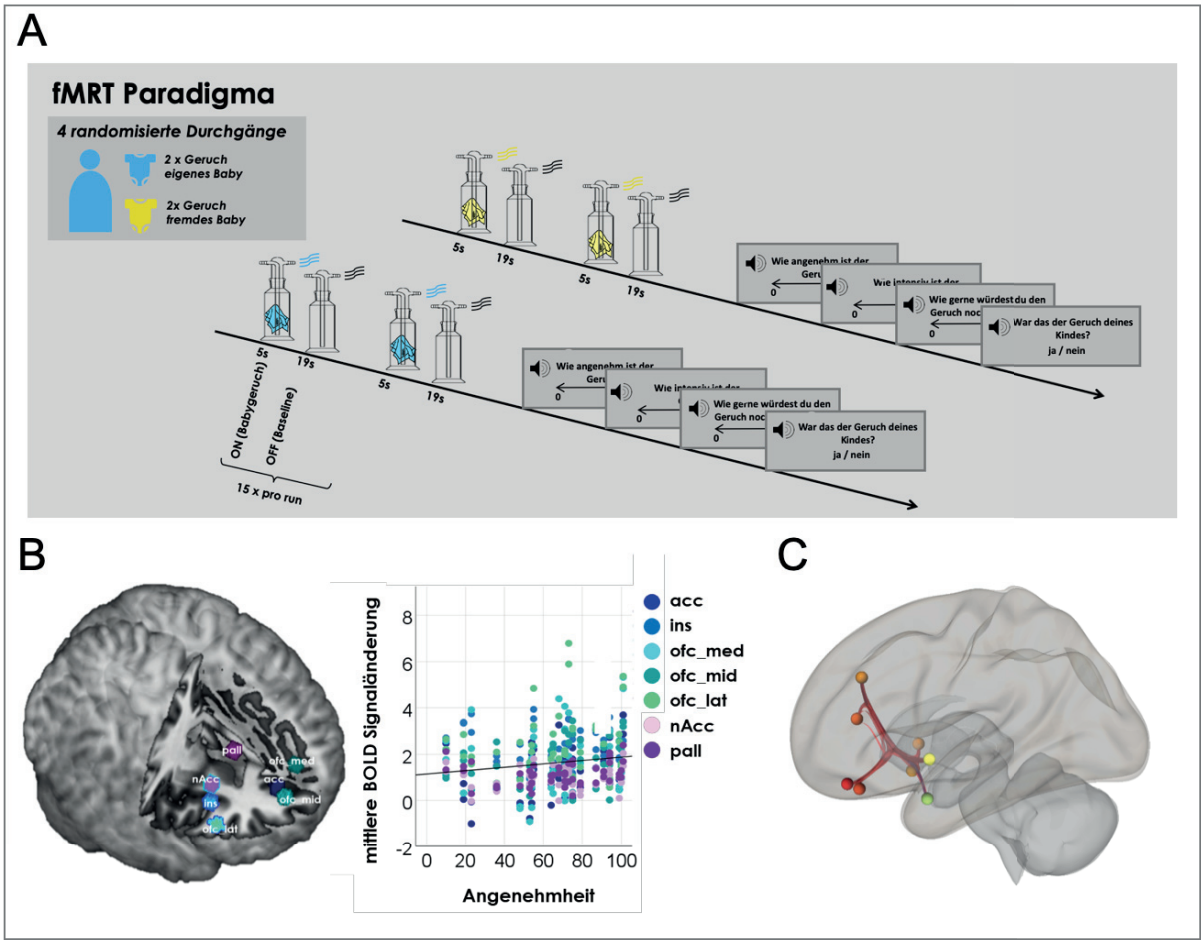

Abbildung 1. A. fMRT Paradigma. B. Linke Seite: Peak-Voxel-Aktivierungen im Pleasure-Netzwerk dargestellt für jede Region of Interest (ROI) , XYZ-Koordinaten basierend auf MNI-space: dunkelblau - acc (anteriorer cingulärer Kortex; [0 42 -2]); hellblau – ins (Insula; [34 20 6]); cyan - ofc_med (medialer Orbitofrontalkortex; [2 -48 -4]); grünblau - ofc_mid (mittlerer anteriorer Orbitofrontalkortex; [-30 36 -14]); hellgrün - ofc_lat (lateraler Orbitofrontalkortex; [38 26 -4]); rosa – nAcc (Nucleus Accumbens; [12 8 -6]); violett – pall (Globus Pallidus; [-12 6 -2]). Rechte Seite: Mittlere BOLD-Signaländerung (Beta-Werte des Kontrasts auf Individualebene (1st Level; Geruch eigenes Baby vs. Baseline) extrahiert für eine 4mm- Sphäre um den Peak-Voxel für jede definierte ROI (XYZ-Koordinaten: siehe oben), in Abhängigkeit der subjektiv bewerteten Angenehmheit des Geruchs (von 0 "überhaupt nicht angenehm" bis 100 "sehr angenehm"). C.ROI-ROI Korrelationen des Pleasure-Netzwerks über die Bedingung Babygeruch vs. Baseline, *N* = 38 Mütter; die Farben stellen T-Werte der Verbindungsstärke dar (grün – rot = niedrig – hoch).

Wie Lundström et al. (2013) und Nishitani et al. (2014) demonstrierten, reagierten Frauen ohne Kinder anders auf die präsentierten Babygerüche als Mütter. Hier ist jedoch zu beachten, dass nicht der Geruch des eigenen, sondern der eines unbekannten Babys präsentiert wurde, weshalb ein spezifischer Effekt des eigenen Babys nicht abgebildet werden konnte. Aus diesem Grund ist es wichtig, den Vergleich von Müttern vs. Frauen ohne Kinder sowie den Vergleich verschiedener Stimuli (Körpergeruch des eigenen Babys vs. des

fremden Babys vs. eines pubertären Kindes) einzubeziehen, um statusabhängige und altersspezifische Effekte zu kontrollieren. Die Hypothese, dass anhand von Babygerüchen tatsächlich ein „olfaktorisches Kindchenschema“ transportiert wird, welches global Niedlichkeit vermittelt, wurde anhand dieser zusätzlichen Kontrollbedingungen in einer weiterführenden fMRT-Studie dieses Projekts untersucht und befindet sich aktuell noch in der Auswertung. Die Ergebnisse sollten allerdings für zukünftige Fragestellungen berücksichtigt werden.

Darüber hinaus liefert die oben genannte fMRT-Studie dennoch Hinweise auf einen spezifischen Effekt, der durch den Geruch des eigenen Babys vermittelt wird: Die Stärke der Aktivierungen im Pleasure-Netzwerk sagte die subjektive Angenehmheitsbewertung des eigenen Kindes vorher: Je ausgeprägter die neuronale Aktivität, desto angenehmer wurde der Körpergeruch des eigenen Babys bewertet (s. Abbildung 1B), was als weitere Evidenz für die Relevanz kindlicher Körpergerüche innerhalb der Mutter-Kind-Beziehung gedeutet werden kann (Schäfer et al., 2019).

Neuronale Korrelate von Bindung – Ausblick

Aktuelle Studien zu neuronalen Korrelaten der Eltern-Kind-Beziehung berichten von weiteren Netzwerken, die hinsichtlich der Bindung relevant sind (Swain, 2011). Auch hier könnten zukünftige Studien untersuchen, ob diese ebenso in Reaktion auf olfaktorische Stimuli existieren. Besonders wichtig ist zudem die Einbeziehung von Vätern: Im Rahmen der Bindungsforschung rücken Väter als primäre Bezugsperson zunehmend in den Fokus, was im Kontext gesellschaftlicher Veränderungen von Rollenbildern und Aufteilung der Erziehung enorme Relevanz hat (Combs-Orme & Renkert, 2009; Lamb, 2000). Es wird angenommen, dass die bindungsspezifische neuronale Aktivität bei Vätern mit der Zeit korreliert, die gemeinsam mit dem Kind verbracht wird (Abraham et al., 2014). Außerdem scheint es eine Biosynchronizität zwischen Müttern und Vätern zu geben: Beim Beobachten von Videos über die Interaktion mit dem eigenen Baby zeigte sich synchrone Hirnaktivität innerhalb einer Mutter-Vater-Dyade in Strukturen, die für soziale Kognition wichtig sind. Dies spricht dafür, dass elterliche Bindung sich auch im Kontext der Partnerschaftsbindung formt (Atzil, Hendler, Zagoory-Sharon, Winetraub, & Feldman, 2012). Bisher wurden vor allem visuelle Stimuli hinsichtlich neuronaler Korrelate der Vater-Kind-Bindung untersucht (Abraham et al., 2014; Atzil et al., 2012). Die Wirkung von Babygerüchen auf das väterliche Gehirn wurde nun erstmalig in unserer Arbeitsgruppe überprüft und kann nach Abschluss der Analyse Aufschluss darüber geben, ob diese, wie bereits bei Müttern beobachtet, neuronal vermittelte Belohnung auslösen.

Generelle Limitationen

Der mögliche Einfluss eines Halo-Effekts (Nisbett & Wilson, 1977) ist als Limitation zu erwähnen, die im Rahmen der Studien aufgetreten sein könnten. Die Eltern wurden zur Studie mit dem Titel „Körpergerüche im Rahmen der Eltern-Kind-Beziehung“ eingeladen, und instruiert, verschiedene Körpergerüche inklusive der ihrer eigenen Kinder zu bewerten. Auch wenn die Versuchsleiterin sagte, dass die weiteren Geruchsproben aus anderen Altersgruppen und auch von Erwachsenen stammen können, ist zu vermuten, dass das Setting die Probandinnen hinsichtlich ihrer Erwartungen beeinflusste. Insbesondere, da die olfaktorische Wahrnehmung sehr anfällig für Labeling-Effekte ist (Herz, 2003). Dies könnte auch dazu führen, dass die Mütter eher dazu tendierten, die Gerüche als präpubertär zu klassifizieren. Hier wäre ein Vergleich mit Frauen, die keine Kinder haben und nicht im Rahmen des Eltern-Kind-Settings instruiert wurden, nötig, um mögliche Kontexteffekte auszuschließen.

In dieser Arbeit wurden T-Shirts bzw. Bodies verwendet, um den Körpergeruch spezifisch durch den Achselgeruch zu erfassen. Subjektiv scheint jedoch auch die Wahrnehmung des Geruchs am Kopf, insbesondere bei jüngeren Kindern, bedeutsam zu sein (Okamoto et al., 2016), weshalb wir in einer aktuellen Untersuchung überprüfen, wie die Wahrnehmung von Körpergerüchen, die von verschiedenen Körperstellen stammen, miteinander korreliert. Die daraus entstehenden Resultate sollten in die Planung zukünftiger Studien einfließen.

Negatives und positives olfaktorisches Imprinting?

Die erste Veröffentlichung zeigt, dass Mütter im Zeitraum der frühen Pubertät den Körpergeruch ihres Sohnes negativer bewerten, wenn der Testosteronspiegel steigt. Ähnliches berichten auch Weisfeld et al. (2003): In ihrer Studie präferierten Mütter den Geruch fremder Kinder gegenüber dem des eigenen unabhängig vom Geschlecht des Kindes, Väter zeigten diese Aversion nur hinsichtlich ihrer Töchter (und andersherum). Auch wenn die Untersuchung eine breitere Altersspanne abdeckte (6-15 Jahre), erfasste sie Kinder am Übergang zwischen prä- zu pubertärer Phase. Insgesamt unterstützen diese Befunde damit die Hypothese, dass negatives olfaktorisches Imprinting zwischen Eltern-Kind-Paaren zu Beginn der Adoleszent auftritt. Bislang ist unklar, wie ein solcher Mechanismus des negativen Imprintings biologisch vermittelt wird. Imprinting wird als „Prozess der Aneignung einer biologischen sozialer Reaktionen auf Artgenossen“ beschrieben (Lorenz, 1937), der in einer bestimmten, sensiblen Entwicklungsphase auftritt (Immelmann, 1975). Dieses Konzept wurde auf verschiedene Dimensionen ausgedehnt, wie z. B. kindliches Imprinting (kindliches Erkennen der Eltern und Bildung einer Bindung) oder sexuelles Imprinting, d.h. entweder positive (Präferenz) oder negative (Vermeidung) Reaktionen auf ein Individuum (Rantala & Marcinkowska, 2011) und wird vermutlich durch olfaktorischen Mechanismen mediiert (Schneider & Hendrix, 2000). Bei Tieren entsteht

olfaktorisches Imprinting oftmals in Reaktion auf endokrinologische Veränderungen, z. B. erhöhtes Estradiol oder Progesteron (Hudson, 1993), kann aber auch über spezifische MHC-Peptide vermittelt werden (Hinz et al., 2013). Bei Menschen wird Imprinting auf phänotypische Eigenschaften und ebenso auf olfaktorisch mediierte Prozesse zurückgeführt, die z. T. mit dem HLA-System in Verbindung gebracht werden (Rantala & Marcinkowska, 2011). Veröffentlichung 1 zeigte hinsichtlich des HLA-Profils eine Bevorzugung des genetisch ähnlichen Geruchs über alle Altersgruppen, was der aus Studien zur Partnerwahl beobachteten Bevorzugung genetisch unähnlicher Körpergerüche widerspricht (Sorokowska et al., 2018). Nachfolgende Analysen der Subgruppen im Anschluss an die Veröffentlichung veranschaulichten in diesem Zusammenhang, dass die Bevorzugung des HLA-ähnlichen Kindes vor allem für die jüngste Altersgruppe (0-3 Jahre), nicht jedoch für pubertäre Kinder (9-13 Jahre) galt. Außerdem konnte durch die vorliegenden Ergebnisse erstmals gezeigt werden, dass die Steroidhormonkonzentration mit einer Aversion zwischen Müttern und Söhnen in der frühen Pubertät assoziiert ist. Dies spricht für ein hormonell vermitteltes negatives olfaktorisches Imprinting (im Sinne der Vermeidung von Sexualkontakt mit dem eigenen Kind). Die Aussagekraft dieses Ergebnisses ist dennoch durch die Stichprobenanzahl in dieser Phase limitiert (N = 21 Mutter-Sohn-Paarungen), weshalb eine Überprüfung anhand einer größeren Kohorte notwendig ist. Zusätzlich ist diese Altersgruppe sehr heterogen im Sinne des Entwicklungsstadiums (s. Veröffentlichung 2), was es bei dieser Stichprobengröße erschwert, präzise Aussagen über den Zusammenhang zwischen mütterlicher Geruchsbewertung, pubertärem Status und Hormonspiegel sowie einem eventuellen Einfluss von genetischer Ähnlichkeit zu treffen. Ferner wurde zwar bei den Müttern, nicht jedoch bei den teilnehmenden Mädchen, für die Zyklusphase und die Einnahme hormoneller Kontrazeptiva kontrolliert, was die mütterliche Angenehmheitsbewertung ebenso wie weitere konfundierende Variablen (z. B. Riechschwelle und Geruchspräferenzen auf Seiten der Mütter; Essgewohnheiten auf Seiten der Kinder) verzerren könnte. Dies sollte in nachfolgenden Studien berücksichtigt werden. Außerdem können aufgrund des querschnittlichen Designs nur korrelative Zusammenhänge dargestellt werden. Hier wäre eine längsschnittliche Untersuchung mit Vätern und Müttern geeignet, um intraindividuelle und geschlechtsspezifische Veränderungen in der elterlichen Wahrnehmung sowie im Körpergeruch über das kritische Zeitfenster des Übergangs zur Pubertät hinweg abzubilden. Auf diese Weise könnten generelle Aussagen über ein negatives olfaktorisches Imprinting in der Eltern-Kind-Beziehung abgeleitet werden. Zusätzlich können chemosensorische Profilanalysen der Körpergerüche in verschiedenen Entwicklungsphasen Erkenntnisse darüber vermitteln, welche molekularen Bestandteile die Veränderung des Körpergeruchs bestimmen (Uebi et al., 2019).

Weiterhin wirft diese Doktorarbeit die Frage nach der Existenz eines *positiven* olfaktorischen Imprintings in den ersten Lebensjahren auf. Die bisherigen Ergebnisse zeigen eine Diskrepanz zwischen der Verhaltens- und der neurobiologischen Ebene: Während im Verhalten eine implizite Präferenz für den Geruch des eigenen Kindes beobachtet wurde, konnte dies neuronal nicht abgebildet werden: Die Aktivierungen in Reaktion auf den Geruch des eigenen vs. des fremden Babys unterschieden sich nicht signifikant. Wie Veröffentlichung 3 deutlich macht, lösen Körpergerüche trotz eines methodisch optimierten Designs nur schwache Effekte auf neuronaler Ebene aus, weshalb subtile Unterschiede vermutlich nur schwer zu detektieren sind. Außerdem erschwert es die komplizierte Geruchsdarbietung im MRT, eine ähnliche Intensität der Gerüche zu gewährleisten, die mit der unmittelbaren Präsentation der Körpergerüche außerhalb des Scanners vergleichbar ist. Veröffentlichung 1 zeigt, dass die Geruchsbewertung genetisch ähnlicher Kinder sich nicht von der des eigenen Kindes unterscheidet. Wie oben bereits erwähnt, zeigte eine weiterführende Datenanalyse, dass dieser Effekt vor allem auf der jüngsten Altersgruppe beruhte und im Laufe der ersten drei Lebensjahre abnahm. Hier stellt sich die Frage, ob positives olfaktorisches Imprinting zwischen Mutter und Kind vorliegt, und wenn ja, in welchem Zeitraum dies auftritt - z. B. nur kurz nach der Geburt, im Sinne einer besonderen Sensitivität für einen genetisch ähnlichen Geruch, um den initialen Bindungsaufbau zu fördern. In der vorgestellten weiterführenden fMRT-Studie wurden Kinder bis zu drei Jahren eingeschlossen, weshalb eventuell eine Verschleierung des Effekts aufgrund der breiten Altersspanne vorlag. In einem Anschlussprojekt soll daher bei Müttern mit Kindern über das erste Lebensjahr im Langzeitverlauf (zunächst auf Verhaltensebene) intraindividuell untersucht werden, ob die genetische Ähnlichkeit tatsächlich die Bevorzugung des Geruchs vermittelt, und, wenn ja, in welchem Zeitraum dies beobachtbar ist.

Klinische Implikationen

Die in der vorliegenden Arbeit gewonnenen Erkenntnisse helfen dabei, biologische Grundlagen der Mutter-Kind-Bindung zu verstehen. Darauf basierend können langfristig Interventionen abgeleitet werden, die sich positiv auf die Eltern-Kind-Bindung auswirken. Bezüglich der neurobiologischen Verarbeitung der Körpergerüche ist die Entwicklung eines Neurofeedback-Trainings vorstellbar, das Müttern mit Bindungsschwierigkeiten hilft, die auf neuronaler Ebene abbildbaren positiven Effekte kindlicher Signale zu fördern. Dies wird aktuell im Rahmen visueller Stimuli erprobt (Eckstein et al., 2019) und könnte auf Chemosignale ausgeweitet werden.

Die Ergebnisse bezüglich Präferenz und Identifikation des Körpergeruchs des eigenen Kindes weisen darauf hin, dass die Vertrautheit ein wesentlicher Faktor ist, der die Wahrnehmung beeinflusst (Delplanque et al., 2008). Daher könnten Interventionen mit dem

Ziel geschaffen werden, die Vertrautheit zwischen Eltern und Kind auf chemosensorischer Ebene zu erhöhen, und auf diese Weise einen positiven, sich selbst verstärkenden Kreislauf auszulösen, der sich auf andere Sinneskanäle ausweitet (Doucet et al., 2007). Dies kann außerdem zugunsten des Kindes genutzt werden. Auch wenn, wie oben berichtet, vereinzelte Studien zeigen, dass die Exposition mit einem vertrauten Geruch förderlich hinsichtlich der Stressreduktion wirkt und bei Frühchen z. B. mit verstärkter Nahrungsaufnahme korreliert, gibt es bislang nur wenig Transfer solcher Interventionen in die klinische Praxis. Für diesen Transfer ist es wichtig, die Integration mehrerer Sinnesmodalitäten zu betrachten, die häufig zu einem wechselseitig intensivierenden Effekt führt (Thesen, Vibell, Calvert, & Österbauer, 2004). Insbesondere die Interaktion zwischen olfaktorischer und taktiler Wahrnehmung ist hier zu nennen – aus Tierstudien ist bekannt, dass diese wesentlich für den frühen Bindungsaufbau ist (Fleming, O'Day, & Kraemer, 1999). Beide Sinne reifen früher als andere sensorischen Systeme (Graven, 2004) und auch Untersuchungen aus dem Humanbereich demonstrieren ihre Bedeutsamkeit für die frühkindliche Entwicklung (Modrcin-Talbott, Harrison, Groer, & Younger, 2003; Yildiz et al., 2011). Die Kombination von olfaktorischen und taktilen Reizen wird z. B. bei der *kangaroo mother care*-Technik angewendet und wirkt schmerzreduzierend bei Frühgeborenen, während eine zusätzliche akustische Stimulation keine additive Wirkung zeigt (Johnston et al., 2009). Solche Erkenntnisse sollten in die Entwicklung zukünftiger Interventionen einfließen, um die Förderung der frühen Eltern-Kind-Beziehung optimal zu gestalten.

Schlussfolgerung

Die vorliegende Arbeit veranschaulicht, dass kindliche Körpergerüche wirksame Chemosignale in der Mutter-Kind-Beziehung darstellen. Die mütterliche Identifikation sowie Präferenz für den Geruch des eigenen Kindes zeigen, dass der kindliche Körpergeruch als biologischer Stimulus zur Initiierung und Aufrechterhaltung der Beziehung beitragen kann. Auch die genetische Ähnlichkeit ist hierbei bedeutsam. Während der frühen Pubertät verändert sich die mütterliche Wahrnehmung und der Geruch des eigenen Kindes wird weder erkannt noch bevorzugt. Bei Söhnen war dies mit dem Anstieg von Steroidhormonen assoziiert. Im postpubertären Stadium kehrt die Identifikation und die Bevorzugung des Geruchs des eigenen Kindes zurück, was für den Einfluss der Vertrautheit auf die Geruchsbewertung spricht.

Generell tendieren Mütter dazu, kindliche Körpergerüche als präpubertär einzuordnen. Für die Klassifizierung des Entwicklungsstadiums anhand des Körpergeruchs sind insbesondere die hedonische Bewertung und der pubertäre Status des Kindes ausschlaggebend. Um herauszufinden, welche Komponenten im Körpergeruch die veränderte Wahrnehmung über die Entwicklung vermitteln, sollten chemosensorische Profilanalysen erfolgen.

Auch auf neuronaler Ebene zeigt sich die Bedeutsamkeit kindlicher Körpergerüche für die Mutter-Kind-Beziehung. Ein methodischer Vergleich zweier fMRT-Paradigmen konnte zeigen, dass kurze, kontinuierliche Stimuluspräsentation mit Babygerüchen stärkere neuronale Aktivität im mütterlichen Gehirn hervorruft, als wenn die Gerüche über einen längeren Zeitraum intermittierend dargeboten werden. Darüber hinaus aktiviert die Wahrnehmung des Babygeruchs belohnungsbezogene Hirnareale sowie das Pleasure-Netzwerk, welches Niedlichkeit vermittelt. Zukünftige Arbeiten sollten diese Ergebnisse aufgreifen und die Spezifität neuronaler Aktivierungen im Zusammenhang mit einer präziseren Erfassung der Beziehungsqualität überprüfen, um weiterführende chemosensorischen Mechanismen der Eltern-Kind-Beziehung abzuleiten. Langfristig können auf dieser Basis Interventionen zur Stärkung der Bindungsqualität entwickelt werden.

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THE ROYAL SOCIETY PUBLISHING

Body odours as a chemosignal in the mother–child relationship: new insights based on an human leucocyte antigen-genotyped family cohort

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Mothers are able to identify the body odour (BO) of their own child and prefer this smell above other BOs. It has hence been assumed that the infantile BO functions as a chemosignal promoting targeted parental care. We tested this hypothesis and examined whether children's BOs signal genetic similarity and developmental status to mothers. In addition, we assessed whether BOs facilitate inbreeding avoidance (Westermarck effect). In a cross-sectional design, $N = 164$ mothers participated with their biological children ($N = 226$ children, aged 0–18 years) and evaluated BO probes of their own and four other, sex-matched children. Those varied in age and in genetic similarity, which was assessed by human leucocyte antigen profiling. The study showed not only that mothers identified and preferred their own child's BO, but also that genetic similarity and developmental status are transcribed in BOs. Accordingly, maternal preference of their own child's odour changes throughout development. Our data partly supported the Westermarck effect: Mothers preference of pubertal boys' BOs was negatively related to testosterone for the own son, but not for unfamiliar children.

This article is part of the Theo Murphy meeting issue 'Chemical communication in humans'.

1. Introduction

An affective tight bond between a primary carer and their child provides essential physical and psychological safety, thus ensuring healthy development of the child [1]. The formation of such a bond can be attributed to a large investment of time, emotions, finances and sociability from the carer. The carer's motivation for such investment is facilitated by compelling characteristics of their child, including infantile visual or auditory cues. For instance, a child's relatively large eyes, small mouth and round face, as described in the Kindchenschema, constitute an infantile cue which promotes gentle and social behaviour in the carer (for a review, see [2]) by coding pleasure, motivation and reward in the parental brain [3].

Another potential factor affecting parental investment is genetic relatedness. On average, parents are willing to invest more resources in genetically related than in step-children [4], a behaviour which is likely facilitated by kin recognition. For example, a child's protruding ears might trigger visual kin recognition by means of resemblance and show a parent with relatively large ears that this child belongs to the same family. In fact, facial resemblance affects a parent's level of investment in their child, especially for fathers [5].

Chemosignalling as a cue for parental investment has scarcely been investigated, but the few existing works show that body odour (BO) similarity can increase parental investments by fathers [6]. BO recognition is a significant predictor of positive mothering attitudes and nursing experiences [7] and relates to higher emotional closeness for fathers and lower rate of corporal punishment for mothers [8]. Another group of studies revealed increased preference of odours from close kin and BO identification abilities within families [8,9]. BO preference is mediated by identification ability; in contrast to healthy mothers who are able to identify their own child's odour shortly after birth [9], mothers with impaired bonding to their child can neither identify nor prefer their own child's BO [10]. Whereas the maternal ability is preserved irrespective of whether the child is infantile, pubertal or post-pubertal, there are inconsistencies in paternal olfactory kin recognition across these developmental stages [9,11,12].

A carer's evaluation of their own child's BO changes over time. Parents perceive the BO of infants aged younger than 12 months as pleasant [7] and the odour of their own infant is preferred over those of other infants. Yet, biological cues which support the development of a tight bond between mother and child become less important with increasing age of the child (as in facial characteristics [13]). Likewise, the preference for one's own offspring's odour seems to decline as a function of development, as suggested by two recent questionnaire studies. One revealed that the carer's regard for their own child`s BO continuously decreases between the age of 3 years and adolescence [14], while another showed that mothers of children below 3 years and fathers of children below 1 year old report more frequent intentional affectionate sniffing of their child's BO than parents of older children [15].

The two existing experimental studies which examined a parent's evaluation of their own child's BO in pre- and pubertal stages have revealed conflicting results. Weisfeld *et al.* [12] found in a sample of 21 families that fathers dislike the odour of their pubertal daughters. This study was interpreted in line with the so-called 'Westermarck effect', which describes the lack of sexual attraction between adults who cohabited as children [16,17]. The aversion to familiar, opposite-sex BOs may hence serve as an olfactory mechanism for preventing inbreeding. However, this result was not replicated in a later sample of nine families [11].

BO comprised genetic, developmental and environmental compounds. The latter refers to highly variable environmental influences such as food, hygiene, disease or culture [18]. Developmental compounds are also variable as they change throughout development: the onset of puberty coincides with a rise in steroid hormones including testosterone and oestradiol [19]. Steroid hormones reflect immunological functioning and are therefore considered to signal genetic health of a potential mate [20]. They are not directly responsible for BO composition but transformation of those steroids via skin bacteria leads to an olfactory percept [21]. Testosterone has been suggested to affect BO ratings [22], e.g. in terms of a more intense and more negative evaluation [23,24], but evidence is mixed [25]. Oestradiol was shown to influence olfactory transmitted sexual attraction in mice [26] and facial attractiveness in human [27] but whether it similarly affects human BO ratings has been unclear. Female assessment of male BOs do not seem related to oestradiol concentration [25]. However, female BOs change around the menstrual cycle and are rated as most pleasant by men around ovulation [18], when oestradiol levels peak [28]. It is unknown whether oestradiol concentration mediates the perceived change in BO [18]. Male ratings of women's BO attractiveness is predicted by the women's oestradiol level [29].

By contrast, olfactory kin recognition is presumably based on stable compounds of BO, which may be genetically influenced [30]. Adult relatives, as well as children are recognizable via BO [31,32], so odour-mediated kin recognition may also be important beyond childhood. By excluding relatives, kin recognition helps identify potential mates while avoiding potential disadvantages of inbreeding, such as a reduced offspring fitness [33]. A well-researched part of the genetic profile which impacts BO assessment is the human leucocyte antigen (HLA) System (or Major Histocompatibility Complex, MHC, in animals). The HLA is involved in the body's immune response by activating T cells through the presentation of peptides [34]. HLA molecules function as chemosignals [35] and partially account for genetic variance in BO. Although the interaction of phenotypic and genetic traits in olfactory kin recognition is not yet well understood, it is known that HLA relates to BO perception. Women prefer the BO of men whose HLA system is different (to a certain degree) from their own [36]. On the other hand, people prefer their own odour when it is supplemented by self rather than non-self MHC ligands [37]. Thus, in a non-mating context, this ability may contribute to parental olfactory identification and preference of the own child's BO, especially in ambiguous situations lacking clear indicative cues (e.g. distinguishing between children of the same age with similar hormonal levels).

These lines of evidence suggest that BOs may promote bonding and incest avoidance by triggering an evaluation incorporating genetic (HLA, sex), developmental (e.g. age, hormonal status) and environmental factors. However, previous results on BO perception in the parent–child dyad are mixed and based on small sample sizes. We therefore aimed to examine maternal perception of children's BO during development—from infanthood to adolescence. We hypothesized that (H1) mothers are able to identify their own child's BO and that this identification relates to genetic (HLA) similarity; (H2) mothers prefer the BO of their own child over the BO of other children and that this preference relates to HLA similarity; (H3) preference of the own child`s BO declines after infanthood; (H4) assessed pleasantness of BOs is higher for those probes identified as one's own child. Furthermore, we expect an additional effect during puberty, namely that (H5) the assessed pleasantness for the BO of one's own opposite-sex child (here, sons) decreases as sons' transition across puberty, whereas this preference remains stable for the same-sex child (daughters) and for unfamiliar children.

2. Method

The ethics committee of the University of Dresden (Code: EK 104032015) approved the conduction of the study in accordance with the 'World Medical Association's Declaration of Helsinki'. Written, informed consent was obtained from all participants.

(a) Participants

The sample included 164 normosmic mothers ($M = 37.5$, s.d. = 7.8 years) participating with at least one biological child ($M = 7.6$, s.d. = 5.9 years, $n = 124$ girls, $n = 102$ boys). The children were

grouped into four age groups, representing stages of hormonal development [19]: infants ($n = 38$ girls and 39 boys; aged 0–3 years, $M = 1.18$, s.d. = 0.96), pre-pubertal ($n = 30$ girls and 23 boys; aged 4–8 years, $M = 5.96$, s.d. = 1.37), pubertal ($n = 23$ girls and 21 boys; aged 9–13 years, $M = 10.91$, s.d. = 1.56) and post-pubertal ($n = 33$ girls and 19 boys; aged 14–18 years, $M = 16.00$, s.d. = 1.24). Post-pubertal therefore does not imply that development is completed, but rather that the phase of hormonal changes and main stages of puberty have begun; whereas pubertal status implies that the phase of hormonal changes and main stages of puberty are about to begin. In order to underpin the definition of these categories, we additionally assessed pubertal status by hormonal analyses and the Pubertal Development Scale (PDS, [38], see below). The four age groups were used to match the BO samples and for further analyses (see below). Demographic variables and descriptive statistics for all measures are listed in electronic supplementary material, tables S1 and S2.

(i) Inclusion and exclusion criteria

Biological parenthood of at least one child between 0 and 18 years was required for inclusion in the study. Exclusion criteria included insufficient German language skills, pregnancy and chronic disease or disability of the child. Anosmia and hyposmia also served as exclusion criteria, this being tested with a screening version of the standardized Sniffin' Sticks Step II® (Burghart, Wedel, Germany). Participants had to identify three odours (cinnamon, banana, fish odour) in a 4-alternative forced-choice task. The application of this test is sufficient to assess normosmia ensuring reliable results with a sensitivity of 80.4% and specificity of 84.3% [39]. If the participant could not identify all the three odours correctly, the full identification subtest consisting of 16 odours was performed and participants were excluded if failing to correctly identify at least 12 [39]. In addition, participants were asked if they currently suffer from smell problems (e.g. rhinitis) before starting the experiment in session 2. If the answer was affirmative, they were asked to attend a later appointment after recovery.

In total, 202 families were recruited for this study, of which two were excluded because mothers became pregnant before the second appointment. Thirty-six further families dropped out before the second session because of a 'lack of time' (26 families), 'moving to another city' (two families) or unspecified reasons (eight families). We also attempted to recruit fathers, but these data are not presented as the sample size was insufficient.

(b) Procedure

Participants were recruited with flyers and advertisement among employees of the university hospital, in schools and kindergartens, as well as with personal invitations. After an initial contact was made, inclusion and exclusion criteria were announced via e-mail.

(i) First session

In the first session, mothers and children came to our Lab of the Department of Psychosomatics at the University Hospital, Dresden. The general procedure was explained and exclusion and inclusion criteria were verified. Besides tests of olfactory performance, the mothers completed medical history, demographic and standardized questionnaires (see *Measures*) and the HLA sampling was done (see below). Afterwards, the subjects received the study kit containing all utensils for taking hormone and BO samples at home, detailed oral and written instructions, and a questionnaire to complete after BO sampling (see below). This contained questions about the situation at home (smoking inside the home, pets, number of persons in the room where the child sleeps), the child's medical condition (drug use, e.g. antibiotics; illness) and contamination of the BO sample (e.g. by urine or faeces) on the experimental night. The first session lasted about 30 min.

The samples and the study protocol were collected the following morning. The samples (t-shirt/onesie) were then cut in half and frozen by −25°C for up to eight weeks before the second session [40]. For the onesies worn by younger children, only the upper part was used to avoid contamination with other odours (e.g. urine).

(ii) Second session

Only the mothers came to the second study session. They were instructed to refrain from wearing perfume on the test day, and not to eat or drink coffee 1 h prior to the experiment. Participants completed additional questions about current pregnancy, the day of their menstrual cycle and current use of hormonal contraception. After explaining the procedure, odour assessment took place.

The second session took between 45 and 60 min depending on the number of children of the mother.

(c) Human leucocyte antigen sampling

Mothers and children were instructed to rub the inner skin of each cheek for 60 s with one buccal swab on each side. The study assistant did the sampling of babies. The buccal swabs were then dried for 5 min and stored in an envelope until genetic analysis. The samples were sent to the ASHI-accredited DKMS Life Science Lab (Dresden, Germany) for HLA analysis, which was done based on high-resolution typing including determination of the nucleotide sequence of exons 2 and 3 of HLA-A, -B, -C, -DRB1, -DQB1 and -DPB1 with next-generation sequencing [41,42].

(d) Developmental status

Developmental status was assessed for all children above the age of 4 years. Children were asked to provide an additional saliva sample in order to determine pubertal status via hormonal analysis. For that purpose, they were equipped with a salivette (Salivette®, code blue, SARSTEDT AG & Co. KG, Nümbrecht, Germany) and parents were instructed to explain to the children that they had to chew for 60 s on the salivette until the cotton contained sufficient saliva for laboratory analysis. In order to assess the relationship between BO assessment and levels of steroid hormones, saliva samples were collected in the evening immediately before the test night.

After sampling, the salivette was stored overnight in the fridge and brought back to the laboratory the next morning together with the BO samples. Saliva samples were frozen (−25°C) and then sent to the Dresden LabService GmbH, where the concentrations of testosterone and oestradiol were determined by immuno-assay analyses.

Furthermore, mothers were asked to rate the children's pubertal status with the Pubertal Developmental Scale (PDS, [38]). The PDS contains three questions asking for development of body hair, growth of breast/beard, menarche and voice break and are characterized for each sex with a global score ranging from 0 (puberty has not begun) to 12 (development completed). Evaluation of the German Version of the PDS shows acceptable reliability ($r = 0.64 - 0.69$); and validity (self- versus external assessment, $r = 0.39$ and 0.83; [38]).

(e) Body odour sampling

Parents collected BO samples at home by following a standardized protocol: in the first session, the families received a study kit containing an appropriately sized 100% cotton t-shirt/onesie for each child, which had been recently washed with odourless detergent (Denkmit Vollwaschmittel Ultra Sensitive, dm-drogerie markt GmbH & Co. KG, Karlsruhe, Germany, www.dm.de). In addition, the mothers were provided with the same odourless

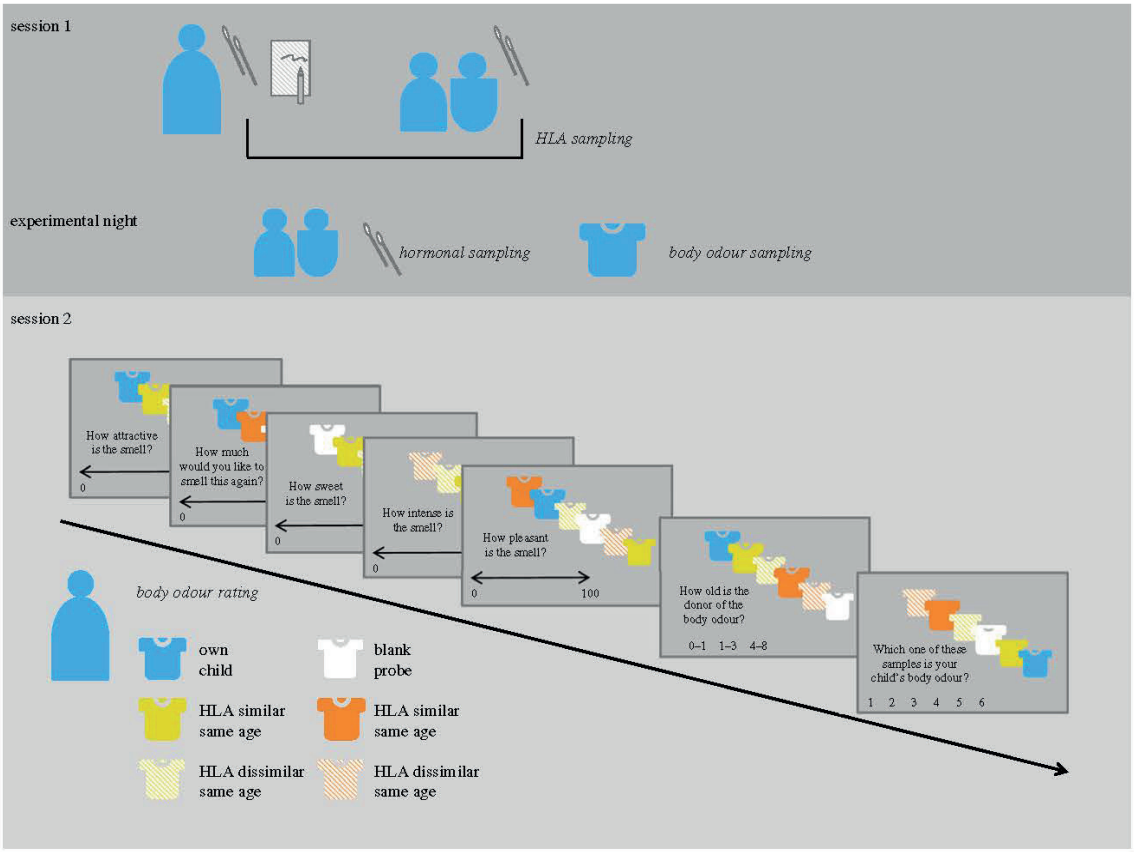

Figure 1. Study design and procedure. Session 1, sampling procedure; session 2, experiment with rating procedure. (Online version in colour.)

detergent, an odourless medical shower gel (both EUBOS flüssig wasch + dusch, Dr. Hobein GmbH, Meckenheim, Germany, www.eubos.de), a re-sealable plastic zip-bag and the questionnaire concerning their conformity with the instructions, which the mothers had to fill in before and after the experimental night. Mothers were instructed to use the odourless detergent to wash any clothes worn in addition to the sample shirt, as well as the child's bedsheets, prior to the experimental night. Further, mothers were instructed to wash their children with the odourless shower gel in the evening and to refrain from using any perfumed hygiene products. On the following morning, the shirt/onesie was stored in the plastic zip-bag and delivered to the laboratory. When this would take longer than 2 h, subjects were instructed to cool the BO sample until it was brought to the laboratory.

(f) Experiment: body odour matching and rating

(i) Body odour matching

Prior to the experiment, the mothers' HLA profiles were matched to the HLA of four unfamiliar children (all sex-matched to the own child). Each mother was matched to two unfamiliar children of the same age group as the own child (one HLA-similar and HLA-dissimilar child) and to two of a different age group as the own child (each one HLA-similar and HLA-dissimilar child, both similarly older or younger than the mother's own child; figure 1). HLA similarity was defined as a match in at least one allele in the loci HLA-B and/or -C (similar = 1–4 matches, see electronic supplementary material, supplementary information on BO matching), while HLA dissimilarity was defined as no matches at HLA-B and/or -C, in accordance with previous studies [43,44]. In the statistical analysis, the HLA influence is referred to as 'BO probe'.

(ii) Body odour rating

Participants had to rate six BO probes: the BO of the own child and four additional, sex-matched BO samples (see above), as well as a blank probe (an unworn *t*-shirt washed beforehand with the same odourless detergent and stored in a plastic zip-bag). The blank probe was used as a control for sufficient intensity of the BO samples.

The samples used for the trial were defrosted 1.5 h before starting the experiment. The study assistant wore odourless rubber gloves and refrained from wearing perfume in order to not bias the odour perception of the participant. First, we conducted a test trial, in which each probe was presented without any assessment in order to ensure anchoring of the stimuli intensity. Afterwards, each BO sample was presented seven times in randomized sequence (5× hedonic ratings, 1× age group rating, 1× identification of the own child, figure 1) and after each presentation, participants assessed one of a total of seven ratings.

At the beginning of each trial, the study assistant instructed the mother to close her eyes during 6 s of smelling. Then, the study assistant held each sample for 6 s with the armpit part upwards directly under the nose of the subject. Afterwards, each sample was placed back, and the mother was instructed to open her eyes and to rate the stimulus. Closing the eyes facilitated concentration and hindered mothers from seeing if the sample was part of a *t*-shirt or of an onesie, which would provide information on the age group of the child.

The ratings included five hedonic (pleasantness, intensity, reward value (wanting), sweetness, attractiveness) and two identification dimensions (identification of the respective age group of the BO donor; identification of the own child's BO, figure 1). Ratings were carried out using visual analogue scales (VAS) ranging from 0 ('very unpleasant', 'not intense at all', 'I don't want to smell this again at all', 'not sweet at all', 'not

attractive at all') to 100 ('very pleasant', 'very intense', 'I would love to smell this odour again', 'very sweet', 'very attractive'). For age group assessment, the subjects had to choose one out of six age categories: less than 1 year, 1–3 years, 4–8 years, 9–13 years, 14–18 years, greater than 18 years. In the last trial, mothers judged which of the BO samples belonged to their own child. This was the only trial, in which the odours were presented twice when the subject asked for a repetition. Afterwards, a pleasant (orange) and an unpleasant odour (fish) were presented serving as odour controls for hedonics of olfactory ratings. On average, orange ($M = 79.05$, s.d. = 20.08) was significantly better rated as fish ($M = 11.20$, s.d. = 15.95; $t_{225} = 43.79$, $p < 0.001$).

(g) Measures

(i) Sociodemographic status

To assess sociodemographic status, subjects were asked to state age, sex, immigration status, highest school-leaving qualification, professional qualification and degree, sexual orientation (hetero-, homo- or bisexual), relationship status (partnership with biological parent of the child, partnership with a new partner, no partnership), number of children, number of biological children, age and sex of each child.

(ii) Medical and psychological status

To assess medical status, subjects were asked to state disease status, alcohol and smoking status, exposure to gas/chemicals, and smell problems. In addition, mothers were asked to provide information about pregnancy or birth complications, preterm birth, disability or serious disease of the child.

Depression score. As depression can affect olfactory performance (for a review, see [42]), this was controlled by the 'Beck Depression Inventory II' (BDI-II, [43]), a widely used questionnaire for evaluating the severity of depression.

Behavioural Inhibition and Activation. In order to measure the mothers' general reward perception, the Behavioural Inhibition and Activation System Scale was assessed [44]. The questionnaire consists of 24 items with a 4-point scale (1 = strong disagreement, 4 thinsp;= strong agreement), such as 'When I get something I want, I feel excited and energized'. Scores are summed up to four subscales indicating Behavioural Inhibition System, Behavioural Activation System (BAS) Reward Responsiveness, BAS Drive and BAS Fun Seeking. The scales show sufficient internal consistency ($\alpha = 0.65$–0.83 [45]).

Participants completed additional questionnaires on the mother–child relationship, which were not the focus of this study.

3. Statistical analyses

All data were analysed with IBM SPSS Statistics 25 (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp).

(a) H1: mothers are able to identify their own child above chance and identification relates to human leucocyte antigen similarity

Here χ^2-tests and binomial tests were used to compare the identification performance to the distribution by chance for each BO probe, and between and within the age groups.

(i) Identification across all children

A one-sample χ^2-test assessed the overall observed distribution against the distribution expected by chance (1/6 = 16.7% for each BO probe). Subsequently, the distributions for each BO probe (own child, HLA-similar child same age, HLA-dissimilar child same age, HLA-similar child different age, HLA-dissimilar child different age) were assessed with binomial tests (versus chance level). Additionally, we tested whether mothers differed in identification performance depending on the sleeping environment (children sleeping in the same room versus in the same bed versus in a different room), but this did not influence identification performance ($\chi^2_2 = 1.84$, $p = 0.398$).

(ii) Identification by age groups

The interaction effect between correct identification (yes versus no) and age group (0–3 years, 4–8 years, 9–13 years, 14–18 years) was analysed. For further exploration, binominal tests were calculated testing the observed distribution against the distribution expected by chance for each age group separately.

For all subsequent analyses, ratings of the blank BO sample were excluded in order to not overcomplicate the results and to focus on the hypotheses. The blank probe was perceived as significantly less intense than all other BO samples ($t_{225} = 9.72$, $p < 0.001$; intensity blank probe: $M = 36.55$, s.d. = 25.53; intensity averaged across BO samples: $M = 53.88$, s.d. = 14.65). For reasons of brevity, the results of the age ratings are not presented. *Pleasantness* ratings were chosen as the main outcome for analyses of hedonic assessment of the BOs, as this has been a common target in previous human olfactory studies investigating BO perception (e.g. [45]). In order to analyse maternal perception of the children's BOs, we used a generalized linear mixed model (GLM) with *pleasantness* as target of this analysis, in which each mother served as an individual, and each BO probe, as well as each child of the mother (in multiple-children families), served as a repeated measure. The respective effect of interest was then modelled as main and/or interaction effect, as described subsequently in detail for each hypothesis. For H2 and H3, we investigated BO probe and age group in one GLM; the assessed effects are listed below.

(b) H2: Mothers prefer the body odour of their own child over other children and this preference relates to human leucocyte antigen similarity

(i) Preference across all children

Target: pleasantness; main effect of BO probe.

We further calculated a preference score by subtracting the pleasantness scores averaged across all unfamiliar BO probes from the score for the mother's own child's BO probe.

Using Bayesian statistics [46,47], we additionally explored the likelihood of the first parts of H1 (identification of the own child above chance) and H2 (preference of the own over other children), as for these hypotheses basic assumptions about the effect sizes of preference and identification of one's own child are available based on a previous publication [10]. For further information, see electronic supplementary material (Bayesian analyses).

(c) H3: The preference of the own child's body odour declines after infanthood

(i) Preference by age groups

Target: pleasantness; main effect of age group of the child (1: 0–3 years, 2: 4–8 years; 3: 9–13 years; 4: 14–18 years); interaction effect between BO probe × age group.

Subsequently, the maternal preference score was tested within age groups (binomial test: preference score versus 0 (greater than 0 = preference)) in order to explore preferences tor their own child's BO in each age group. In addition, we compared pleasantness ratings of the control odours (orange, fish) between the age groups with a repeated measures ANOVA controlling hedonic perception across the different age groups.

(d) H4: The assessed pleasantness is higher for those body odour probes identified as the own child

In addition, we explored whether maternal pleasantness perception was related to the BO sample chosen as the 'own child' (chosen probe = yes/no, irrespective of false or correct choice).

(i) Pleasantness by identification

Target: pleasantness; main effect: chosen probe (yes/no); twofold interaction effects: BO probe × chosen probe, age group × chosen probe.

(e) H5: The assessed pleasantness for the body odour of the own opposite-sex child (sons) decreases with increase of the sons' developmental status whereas the assessed pleasantness remains stable for the same-sex child (daughters)

For assessment of the hypothesized decline in maternal pleasantness ratings for their son's BO during development, we included only children above the age of 4 years (pre-pubertal, pubertal and post-pubertal age group) in an ANOVA with the preference score as target. For each developmental marker (pubertal status (pds score), hormonal status (testosterone, oestradiol)) and each sex, two models assessed the following interactions:

Girls: pds score × age group, oestradiol × age group
Boys: pds score × age group; testosterone × age group

In order to ensure robust distribution for statistical analyses, we log-transformed the hormonal data with lg(10).

Post hoc tests. For all models of H2–H4, pairwise post hoc comparisons were analysed using *t*-tests. Mean values (*M*) and 95% confidence intervals (reported as CI) are presented (electronic supplementary material, table S3). For all models of H5, Pearson Correlation Coefficients served for post hoc bivariate correlational analyses.

4. Results

(a) H1: mothers are able to identify their own child above chance and identification relates to human leucocyte antigen similarity

(i) Identification across all children

The observed distribution of identified BOs differed significantly from the expected distribution by chance ($\chi^2_{224} = 64.64$, $p < 0.001$). The mothers were able to correctly identify the BO of their own child (identification rate: 35.2%; CI: 29–42%). This exceeded the chance level of 16.7% ($p < 0.001$, figure 2*a*).

The HLA-dissimilar same aged child (16.1%, CI: 12–22%, $p = 0.467$) and the HLA-similar same aged child (14.5%; CI: 11–20%, $p = 0.257$) were not chosen above chance and hence no influence of HLA similarity was observed. The identification rate of the blank probe did not exceed chance level (16.2%, CI: 12–22%, $p = 0.345$).

The responses for BOs of children whose age group differed from the one of the own child were below chance (HLA-dissimilar different aged child: 10.1%, CI: 7–14%, $p < 0.001$; HLA-similar different aged child: 7.9%, CI: 5–12%, $p = 0.005$, figure 2*a*).

(ii) Identification by age group

Mothers could correctly identify the BO of their own child in all age groups except puberty (infants: 36.4%, CI: 27–48%, pre-pubertal: 34.6% CI: 24–49%; post-pubertal: 41.1% CI: 29–54%; each $p < 0.001$). For the pubertal age group, the identification of the own child's BO did not differ significantly from chance level (26.2%, CI: 16–42%, $p = 0.062$, figure 2*a*). Bayesian analyses supported the alternative hypotheses (identification of the own child better than chance) over the null hypothesis for age groups of 0–3, 4–8 and 14–18 years. Neither the null nor the alternative hypotheses were supported for the age group of 9–13 years (see electronic supplementary material, table S4).

(b) H2: Mothers prefer the body odour of their own child before other children and this preference relates to human leucocyte antigen similarity

(i) Preference across all children

A significant main effect of BO probe ($F_{4,359} = 5.82$, $p < 0.001$) demonstrated that the own child's BO was rated most pleasant. The mean preference of the own child's BO was 7.1 (CI: 3.86–10.34) higher than for all other probes (figure 2*b*; see electronic supplementary material, table S3). The next-pleasant odour was from the HLA-similar same aged child and the rating for this BO and the own child's BO did not differ significantly ($p = 0.068$; compare table 1). Bayesian statistics favoured the alternative hypotheses (significant preference of the own child's BO compared to unfamiliar children) over the null hypothesis for age groups 0–3, 4–8 and 14–18 years supported the rejection of the alternative hypotheses for the age group of 9–13 years (compare electronic supplementary material, table S5).

(c) H3: The preference of the own child's body odour declines after infanthood

(i) Preference by age groups

There was neither a significant main effect of age ($F_{3,678} = 1.64$, $p = 0.178$) nor a significant interaction effect between age and BO probe on maternal pleasantness ratings ($F_{12,203} = 0.81$, $p = 0.638$). The preference for the own child`s BO was hence above zero in almost all age groups (preference score for infants: *7.62*, CI: 1.1–13.51; pre-pubertal: 9.20; CI: 2.59–15.80; post-pubertal: 8.74, CI: 2.53–14.96, $p = 0.008$ to 0.05). Similar to the identification results, we found no significant preference of the own child in the pubertal age group (*1.61*, CI: −7.19–8.93, $p = 0.652$; figure 2*b*, see electronic supplementary material, table S3).

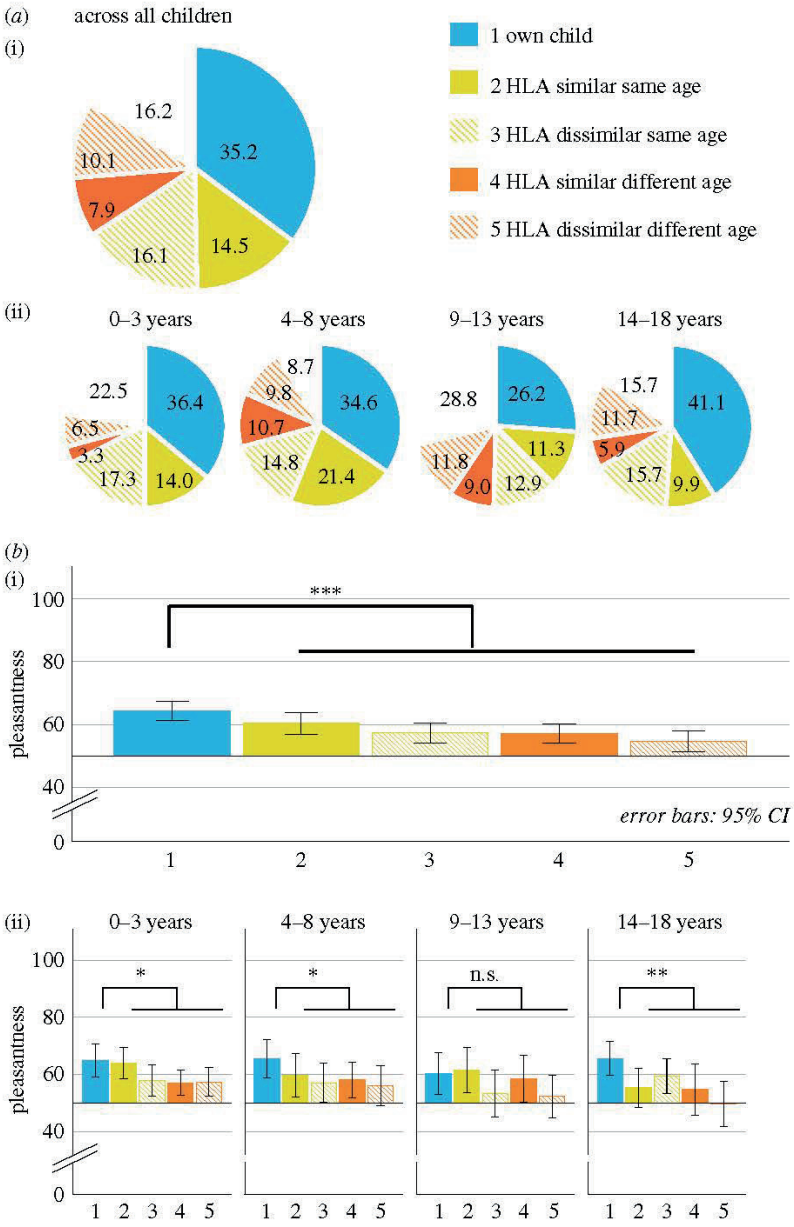

Figure 2. (*a*) Identification of BO probes depicted in % across all children (i) and for each age group (ii). (*b*) Maternal Preference of each BO probe and comparison between own child's BO versus all other samples depicted across all children (i) and for each age group (ii). *$p < 0.05$; **$p < 0.01$, ***$p < 0.001$; n.s. = not significant ($p > 0.05$). (Online version in colour.)

In order to ensure that the reduced pleasantness perception in the pubertal age group was not based on a general reduced hedonic perception of the particular mothers of that age group, we compared pleasantness ratings of the control odours orange and fish and found that the hedonic perception did not differ between the age groups ($F_{3,220} = 1.75$, $p = 0.158$) and that none of the post hoc comparisons were significant.

(d) H4: The assessed pleasantness is higher for those body odour probes identified as the own child

(i) Pleasantness by identification across all children

Mothers rated BO probes chosen as the 'own child' significantly more pleasant ($F_{1,805} = 21.03$, $p < 0.001$) compared to non-chosen BOs, irrespective of whether the choice was correct or false (figure 3*a*).

A significant interaction between BO probe and choice ($F_{8,492} = 2.15$, $p = 0.030$) further showed that BOs chosen as the own child were rated similarly pleasant ($F_{4,181} = 0.64$, $p = 0.932$), but BOs not chosen as the own child differed: Among those non-chosen probes, pleasantness ratings of the own child and the HLA-similar child same aged child were significantly higher than ratings of the other BO probes ($F_{4,925} = 2.49$, $p = 0.042$), without any significant difference between the BO of the own child and the HLA-similar same aged child, $p = 0.641$.

(ii) Pleasantness by identification by age groups

The pleasantness ratings for chosen BOs were higher for BOs of pre-pubertal children ($F_{6,750} = 2.29$, $p = 0.034$): BOs (falsely

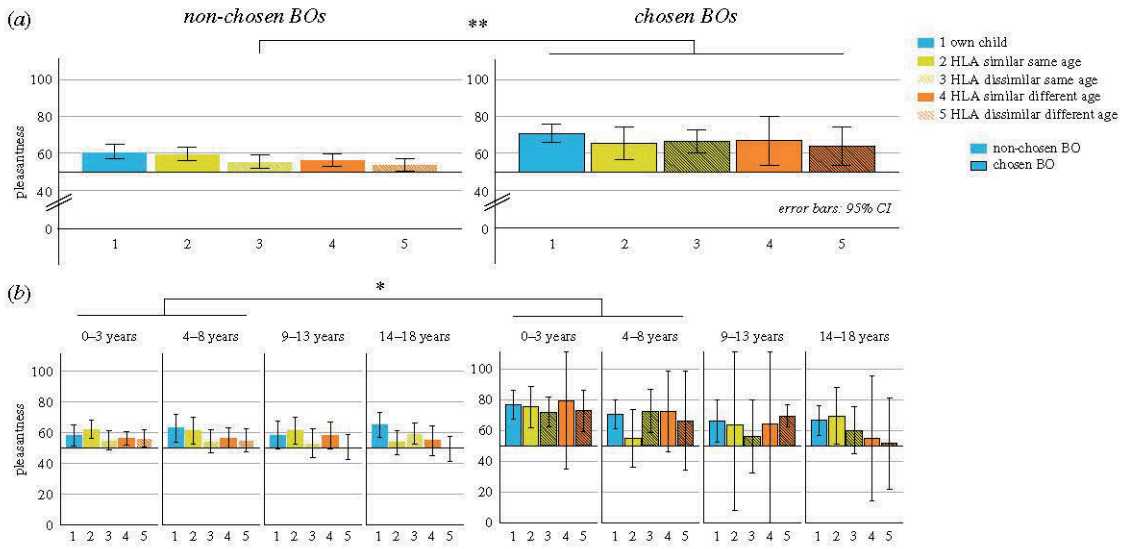

Figure 3. Maternal Preference of BO probes depicted by identification behaviour: A left side: non-chosen BOs, right side: chosen BOs; B: left side: non-chosen BOs depicted by age group; right side: chosen BOs depicted by each age group. *$p < 0.05$; **$p < 0.01$, ***$p < 0.001$. (Online version in colour.)

and correctly) chosen as the own child's BO were rated as more pleasant in the infant and pre-pubertal age groups (0–3 years: 17.17, CI: 11.38–22.96, $p < 0.001$; 4–8 years: 8.69, CI: 1.45–15.90, $p = 0.018$) but not in pubertal and post-pubertal children (9–13 years: 6.37, CI: −1.47–14.13, $p = 0.110$; 14–18 years: 4.66, CI: −3.20–12.52, $p = 0.244$, figure 3*b*, see electronic supplementary material, table S3).

(e) H5: The assessed pleasantness for the body odour of the own opposite-sex child (sons) decreases with increase of the sons' developmental status whereas the assessed pleasantness remains stable for the same-sex child (daughters)

(i) Relationship between developmental status and age

Pubertal status of boys correlated positively with the testosterone level ($r = 0.50$, $p = 0.007$); and likewise, the girls with higher pubertal status exhibited increased oestradiol concentration, $r = 0.33$, $p = 0.015$. In older age groups, a higher level of pubertal status was observed for each boys ($r = 0.77$, $p < 0.001$) and girls ($r = 0.87$, $p < 0.001$). Older age was further associated with increased testosterone levels for boys ($r = 0.51$, $p < 0.001$) and with higher oestradiol levels for girls ($r = 0.27$, $p = 0.026$, electronic supplementary material, figure S1).

(ii) Influence of developmental status on maternal pleasantness ratings

Pubertal status did not relate to maternal preference (girls: pubertal status × age group: $F_{3,55} = 0.67$, $p = 0.572$; boys: pubertal status × age group: $F_{3,37} = 0.22$, $p = 0.880$).

For boys, a significant interaction between testosterone and age group emerged ($F_{3,41} = 3.45$, $p = 0.026$), but not between oestradiol and age group ($F_{3,41} = 0.80$, $p = 0.502$). Subsequent correlational analyses revealed a decrease in pleasantness ratings of own pubertal sons (age group 9–13 years) with elevated testosterone concentration ($r = -0.53$, $p = 0.050$, figure 4). No other significant correlations were observed. For girls, neither a significant effect of testosterone ($F_{3,60} = 0.17$, $p = 0.918$) nor of oestradiol concentration ($F_{3,71} = 1.29$, $p = 0.254$) on maternal pleasantness ratings was observed. Post hoc correlational analyses for each age group showed a positive association between pleasantness ratings of own pubertal daughters (age group 9–13 years) and oestradiol levels ($r = 0.51$, $p = 0.041$). Excluding the outliers (hormonal value of less than or equal to −0.50; figure 4) from the sample, the correlation was no longer significant. No other significant correlations emerged.

5. Discussion

In line with our hypotheses H1 and H2, mothers were able to identify the BO of their own child and preferred this odour above the BO of unfamiliar children. HLA similarity had no major impact on the identification but did affect maternal preference of BOs. As predicted in H3, the preference for their own child's BO declined after infanthood but increased again after puberty. In line with H4, there was a higher preference for BO probes identified as the own child, irrespective of whether this identification was correct. Supporting H5, the maternal preference for the pubertal son's BO, but not for the BO of unfamiliar pubertal boys, decreased with increasing developmental status. In the following paragraphs, these results will be discussed for each hypothesis and then converged in a combined model.

In terms of *kin recognition*, our data confirms previous studies [9,11,12] and demonstrates in a larger sample that healthy mothers can identify their own child's BO consistently throughout development, with the exception of early puberty. Although the identification ability of the present sample was above chance, it was worse compared to previous studies [48]. This might be due to methodological differences (e.g. shorter exposure, more probes to choose, directly worn versus frozen BO samples). In our data, no HLA-related impact on kin recognition was found. Nevertheless, it is possible that a potential influence of genetics drives kin recognition directly after birth and that, over time,

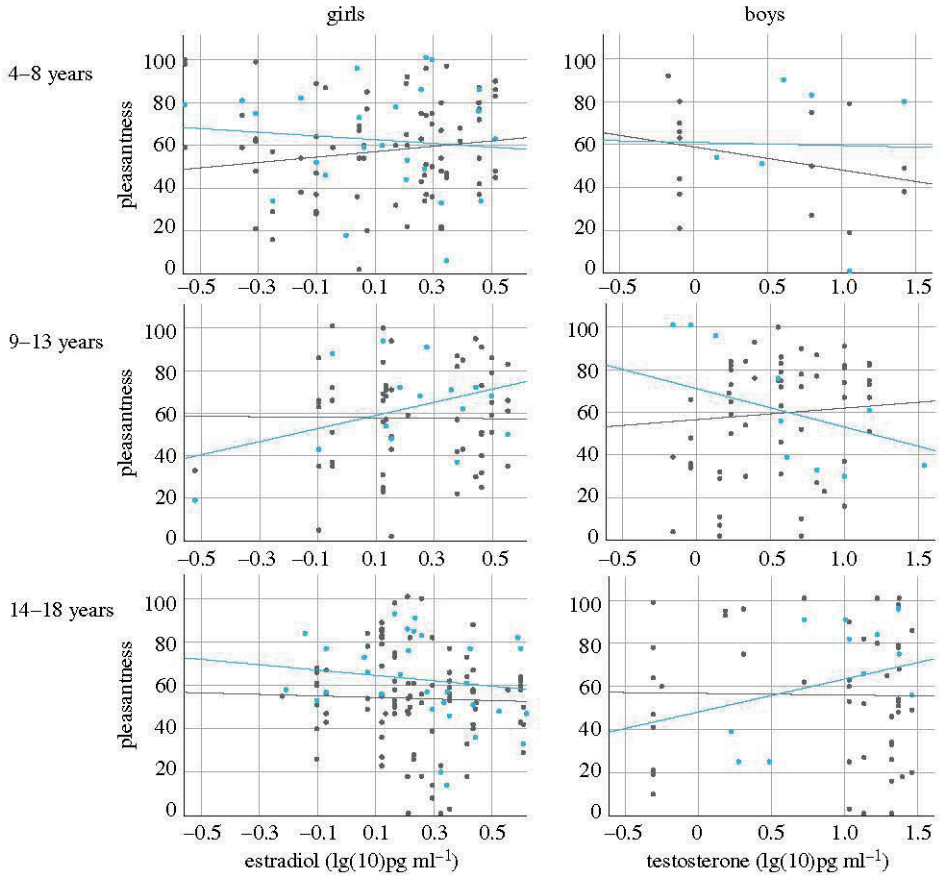

Figure 4. Scatterplots for maternal pleasantness ratings of BOs in relation to hormonal levels depicted by age group and sex of the child. Blue dots, own child; grey dots, unfamiliar child. (Online version in colour.)

environmental compounds overrule this effect. Our study is not suited to test this hypothesis.

We suggest that *familiarity*, the feeling that one has smelled an odour before, contributes to olfactory kin recognition. In general, familiar odours, such as everyday life odours, are identified with higher likelihood [49] and preferred [50], and in the domain of BO, recognition of unrelated individuals is assumed to be mediated by familiarity [12,51]. The inability of mothers to identify their pubertal child fits this approach. During this developmental period, steroid hormones increase, which may consequently increase a child's BO intensity (e.g. [24]). Hence, the child does not smell familiar anymore. In the post-pubertal age group, this effect disappears as the 'new' BO becomes familiar again following prolonged exposure.

In terms of *preference*, mothers preferred the odour of their own child. The next-pleasant odour was the BO of an unfamiliar child who was in the same age group as the own child and HLA-similar to the mother. This supports previous results on the impact of HLA on BO perception [32,37,44] and implies that both developmental and genetic compounds contribute to BO preference. This effect is behaviourally relevant: a higher maternal preference for children with HLA-similar BOs might lead to higher parental investment in such children. This preference effect is reversed in the context of mate choice, where HLA dissimilarity was found to drive BO attractiveness ratings [36], in particular on HLA-B and -C [41] and such dissimilarity between mates enhances fitness of the offspring [33]. Age-related differences in maternal preference are discussed in the overall model below.

Maternal *identification behaviour* mediated the preference of the own child's odour. BO samples chosen as 'own' were strongly preferred over non-chosen probes, irrespective of whether they were the correct or false choice. Interestingly, this finding was most pronounced in the infant and pre-pubertal age group, supporting the idea that identification is a necessary antecedent for bonding, especially during the period where bonding is most crucial for the child [33,52]. The higher preference for chosen versus non-chosen BOs may function as one sensory mechanism enhancing action readiness, which facilitates a prompt reaction for the child's needs, as it has been reported for other modalities [3]. It has been further proposed that BOs function as *instrumental* and *affective* cues in the context of caregiving [15]. Where the instrumental value signals physiological needs (e.g. changing diapers), the affective value of BOs (e.g. reflected in pleasantness perception of the BO [14]) might function as a reward, promoting proximity to the child and, thus, driving emotional attachment. This might be particularly true for infancy and pre-pubertal ages, while pubertal children no longer depend on such intense parental care and attention. In this regard, bonding-related olfactory cues also lose their importance ([14], as compared with visual cues [13]) or change their meaning, e.g. signalling maturity over infantile needs.

According to H5, the *drop in BO ratings for pubertal sons* indicates that elevated testosterone levels during adolescence

are expressed in BO and moderate the mother's perception. For daughters, it is unclear whether we observe the reverse effect: elevated oestradiol levels during puberty lead to an increase in pleasantness ratings. This might be due to either a strong resemblance between the pubertal daughter's BO and the mother's own BO with regard to oestradiol level or to the fact that it is unclear whether oestradiol affects BO perception in a similar way to testosterone [24]. Oestradiol level of the donor has been shown to predict male ratings of women's BO attractiveness [29], and this might apply for female evaluation likewise. However, this was in the context of mate choice, whereas our study focused on the mother–child relationship, which is why context-dependent differences have to be considered. As testosterone and oestradiol concentrations fluctuate within an individual, we sampled the evening before the experimental night, in order to assess the impact on BO. It is not yet understood in detail how chemical compounds released after hormonal changes affect BO composition, but our findings provide further support for their importance for social chemosignalling [18].

Pubertal status, referring mainly to visual characteristics, was naturally related to age and hormonal status. However, the impact of pubertal status on maternal ratings was not significant; we thus surmise that hormonal related olfactory cues do impact BO assessment. We speculate that testosterone functions as a potent olfactory cue, signalling maturity to the mothers. As children enter sexual maturity, inbreeding is possible but should be avoided. Therefore, BOs comprise a natural barrier to reduce the likelihood that mothers would mate with their own child (Westermarck effect, [17]). In the two small experimental studies which exist to date, a mutual aversion of BO in father–daughter dyads in pubertal age but no such phenomenon in mother–son relationships was reported [12] and one study did not find any Westermarck-like effect at all [11]. Our data partly confirm the Westermarck effect, as we observed lower maternal liking for pubertal sons' odour compared to unfamiliar boys. However, incest avoidance does not fully explain our findings as maternal pleasantness evaluation dropped in the early pubertal stage but then recovered for late pubertal BOs. As discussed above, we speculate that these changes in pleasantness might be attributed to regained familiarity over time and, hence, regained pleasantness of son's odour.

We are aware of several limitations of this study. We assessed genetic and developmental compounds, operationalized with HLA and steroid hormones, but did not assess any other genetic compounds and hormones. Despite a rather large power of the overall sample, the sample size for the adolescent children was still small when split for sons and daughters, and not powerful enough to detect small effects. Furthermore, an investigation of the hormonal effects of daughters' BO on paternal perception would be enlightening. We still do not know whether fathers might be more prone to the Westermarck effect, as reported previously [12], although sibling-related studies demonstrate stronger inbreeding aversion for woman compared to men [53].

Taken together, we propose a model explaining maternal perception of their child's BO across age groups, which takes developmental, environmental and genetic compounds of BOs into account (see electronic supplementary material, figure S2). Maternal preference and identification of the own child's odour were *age-related* as they were observed for all groups except puberty. Differences between the age groups might be modulated by different factors which alter BO. Whereas BO preference relates to genetic similarity, kin recognition is based on familiarity, thereby overruling the genetic influence. Both mechanisms may facilitate targeted parental investment when bonding is most pivotal for a child. Developmental compounds play a large role in the critical period of puberty.

In infants and pre-pubertal children, kin recognition and preference of the own child's odour were stable. While kin recognition is presumably based on familiarity, HLA similarity may drive initial BO preference in these age groups as a potential mechanism of olfactory imprinting. The developmental influence of an infant's BO may relate to a perceived 'cuteness' of the BO in that age group, which mothers frequently report [14]. This is supported by the fact that mothers with impaired olfaction report a regret of the lack of that experience [54], and that this infantile smell activates reward areas in the maternal brain [55]. Infant cues elicit activations in hypothalamic, limbic and cortical networks mirroring parenting domains (for a review, see [56]). Infantile facial cuteness activates the pleasure network in mothers [3] indicating that similar effects can be triggered by olfactory cues when perceived as pleasant. Recruitment of this network relates to privileged processing and approach behaviour and thus evokes parental care [3].

In puberty, kin recognition and preference were not present. Both were presumably hindered by the dominant developmental influence of hormonal changes overriding genetics and familiarity: During this developmental stage, the own child's BO is not recognized because it does not smell familiar, and it is not preferred because it smells more intense. In addition, developmental compounds promote olfactory aversion of opposite-sex children, which may facilitate inbreeding avoidance.

In post-pubertal children, kin recognition and preference recovered. We assume that both improved as a function of increased familiarity, due to a longer exposure to the BO and, hence, its evaluation as more pleasant again [50,51].

Further research into olfactory-mediated parental affection could investigate carers with either an impaired sense of smell or an impaired relationship to their child. Although we know that mothers with impaired bonding to their child do not prefer or recognize their child's odour [10], it is unclear whether their poor recognition abilities are a cause or a consequence. Future studies could focus on how differences in maternal behaviour contribute to differences in BO perception. In particular, maternal behaviour could be operationalized by an assessment of the relationship between observations of interpersonal touch or time spent in dyadic interaction and BO perception. The hedonic impact of familiar BOs demonstrates the possibility of clinical interventions supporting mother–child bonding, using olfaction as a promising target for such family interventions. Olfactory training or neurofeedback approaches using exposure to BO may thereby enhance sensory awareness, activate neural networks in response to pleasure, and, in turn, affect approach behaviour and parenting in a positive way.

Ethics. The ethics committee of the University of Dresden (Code: EK 104032015) approved the conduction of the study in accordance with the 'World Medical Association's Declaration of Helsinki'. Written, informed consent was obtained from all participants.

Data accessibility. The datasets supporting this article have been uploaded as part of the electronic supplementary material and by authors on request.

Authors' contributions. I.C., A.S. and L.S. contributed to conception and design of the study. L.S. acquired the data. L.S. and I.C. performed the statistical analysis. L.S. wrote the first draft of the manuscript. I.C. wrote sections of the manuscript and A.S. critically revised the manuscript. J.S. and A.S. conducted the genetic analyses and revised the manuscript. All authors contributed to manuscript revision, read and approved the submitted version.

Competing interests. We declare we have no competing interests.

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PHILOSOPHICAL TRANSACTIONS B

Supplement: Body odours as a chemosignal in the mother-child relationship: new insights based on an human leucocyte antigen-genotyped family cohort

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Keywords: olfaction, parent-child relationship, body odor, MHC, hormones, chemosensory communication

Supplementary information on body odour matching (compare manuscript, method: BO matching):

For the own children, the mean similarity of shared HLA-B and -C alleles between mother and child across the whole sample was 2.2 alleles (SD = 0.53, ranging from 2 – 4 alleles, with 87% sharing 2 alleles, 8 % sharing 3 alleles, and 5 % sharing 4 alleles). For shared HLA-B and -C alleles between mothers and matched body odour (BO) samples across all HLA-similar unfamiliar children, the mean similarity was 1.75 alleles (SD = 0.62; for same aged children: $M = 1.8$, $SD = 0.59$, for the different aged children: $M = 1.65$, $SD = 0.64$; ranging from 1 to 4 alleles, with 36 % sharing 1 allele, 59 % sharing 2 alleles; 3 % sharing 3 and 2% sharing 4 alleles). Between mothers and matched BO samples across all HLA- dissimilar unfamiliar children, similarity was 0, as previously defined.

Supplementary tables

Supplementary Table 1. *Measures: Metrical variables displayed with M, SD, n for each age group and across all children.*

variable	0-3 years			4-8 years			9-13 years			14-18 years			across all		
	M	*SD*	*n*	*M*	*SD*	*n*	*M*	*SD*	*n*	*M*	*SD*	*n*	*M*	*SD*	*n*
number of children	1.42	.72	59	1.88	.64	40	2.09	.68	22	2.02	.60	43	1.79	.72	164
number of biological children	1.38	.56	59	1.82	.63	40	2.09	.68	22	1.98	.56	43	1.75	.65	164
smoking (years) in the past	2.46	1.95	14	2.98	2.81	12	.50	.71	2	1.17	1.47	3	2.30	2.25	34
BDI II	5.66	4.32	59	5.34	4.86	40	5.53	6.94	22	3.91	4.52	43	5.16	5.02	164
BIS score	21.11	3.15	59	22.12	3.32	40	21.41	3.22	22	19.49	3.01	43	21.03	3.28	164
BAS score	39.90	3.82	59	37.94	4.86	40	37.03	4.85	22	37.79	5.10	43	38.56	4.67	164
breastfeeding (in month)	10.45	7.42	52	11.23	6.10	33	11.42	5.38	16	8.35	7.27	30	10.41	6.76	164

Supplementary Table 2. *Measures: Categorical variables displayed with number, %, and n for each age group and across all children.*

variable	**category**	**0-3 years**			**4-8 years**			**9-13 years**			**14-18 years**			**across all**		
		number	*%*	*n*	*number*	*%*	*n*	*number*	*%*	*n*	*number*	*%*	*n*	*number*	*%*	*n*
educational degree	other/primary/ secondary school/ technical school /high school	2/ 0/ 14/ 4/ 39	1.9/ 0/ 24.5/ 7.5/ 66.0	59	0/ 1/ 13/ 0/ 26	0/ 2.9/ 32.4/ 0/ 64.7	40	0/ 0/ 6/ 2/ 14	0/ 0/ 27.3/ 9.1/ 63.6	22	0/ 0/ 14/ 3/ 26	0/ 0/ 32.6/ 7.0/ 60.5	43	1/ 1/ 44/ 11/ 106	.6/ .6/ 26.8/ 6.7/ 64.6	164
school-leaving qualification	apprentice/ completed apprenticeship/training/ technical school/ university of applied science/ University	2/ 6/ 19/ 3/ 3/ 27	1.9/ 9.4/ 32.1/ 5.7/ 5.7/ 45.3	59	2/ 7/ 8/ 2/ 2/ 19	5.0/ 17.5/ 20.0/ 5.0/ 5.0/ 47.5	40	0/ 4/ 7/ 3/ 2/ 6	0/ 18.2/ 31.8/ 13.6/ 9.1/ 27.3	22	0/ 9/ 7/ 8/ 4/ 15	0/ 20.9/ 16.3/ 18.6/ 9.3/ 34.9	43	3/ 25/ 39/ 16/ 11/ 69	1.8/ 15.2/ 23.8/ 9.7/ 6.6/ 42.1	164
university degree	Bachelor/ Magister/ Master/ Diploma/ Diploma university of applied science/ state exam/ phd	5/ 0/ 5/ 5/ 4/ 4/ 4	18.5/ 0/ 18.5/ 18.5/ 14.8/ 14.8/ 14.8	27	2/ 0/ 0 / 11/ 0/ 2/ 6	7.41/ 0/ 0/ 40.7/ 0/ 7.4/ 22.2	21	1/ 0/ 0/ 4/ 2/ 1/ 0	12.5/ 0/ 0/ 50.0/ 25.0/ 12.5/ 0	8	1/ 2/ 0/ 8/ 4/ 3/ 1	5.3/ 10.5/ 0/ 42.1/ 21.1/ 15.8/ 5.3	19	9/ 5/ 3/ 29/ 15/ 10/ 9	11.3/ 6.3/ 3.8/ 36.3/ 18.8/ 12.5/ 11.3	80
sexual orientation	hetero/ homo/ bisexual	57/ 2/ 1	96.6/ 3.4/ 1.7	59	39/ 1/ 0	97.5/ 2.5/ 0	40	22/ 0/ 0	100.0/ 0/ 0	22	42/ 0/ 1	97.7/ 0/ 2.3	43	159/ 3/ 2	96.7/ 2.0/ 1.3	164
relationship status	single/partnership with biological parent/ partnership with new partner	2/ 55/ 2	3.4/ 93.2/ 3.4	59	0/ 35/ 4	0/ 87.5/ 12.5	40	0/ 20/ 2	0/ 56.4/ 43.6	22	7/ 21/ 15	16.3/ 48.8/ 34.9	43	9/ 132/ 23	5.5/ 80.5/ 14.0	164
use of hormonal contraceptive	yes/ no / no	29/ 30	49.1/ 50.9	59	10/ 30	25/ 75	40	6/ 16	27.3/ 72.7	22	17/ 26	39.5/ 60.5	43	53/ 97	35.3/ 64.7	164
accident with head	no/ yes	56/ 3	94.3/ 5.7	59	38/ 2	95.0/ 5.0	40	20/ 2	90.0/ 9.1	22	39/ 4	90.7/ 9.3	43	141/ 11	92.8/ 7.2	164
trauma	no/ yes	59/ 0				91.2/ 8.8		21/ 1	95.5/ 4.5						96.1/ 3.9	
frequent sinusitis	no/ yes	55/ 4	100.0/ 0	59	37/ 3	95.0/ 5.0	40	21/ 1	95.5/ 4.5	22	41/ 2	95.3/ 4.7	43	146/ 6	94.1/ 5.9	164
hayfever	no/ yes	57/ 2	92.5/ 7.5	59	38/ 2	80.0/ 20.	40	22/ 0	100.0/ 0	22	41/ 2	95.3/ 4.7	43	143/ 9	91.4/ 8.6	164
frequent cold		58/ 1	96.2/ 3.8	59	32/ 8	97.5/ 2.5	40	20/ 2	90.9/ 9.1	22	40/ 3	93.0/ 7.0	43	139/ 13	96.7/ 3.3	164
obstructed nasal	no/ yes		98.1/ 1.9	59	39/ 1		40			22	42/ 1	97.7/ 2.3	43	147/ 5		164
breathing	no/ yes	59/ 0				100.0/ 0		21/ 1	95.5/ 4.5						99.3/ .7	
nervous disease	no/ yes	59/ 0	100.0/ 0	59	40/ 0	100.0/ 0	40	22/ 0	100.0/ 0	22	43/ 0	100.0/ 0	43	151/ 1	100.0/ 0	164
jaundice	no/ yes	59/ 0	100.0/ 0	59	40/ 0	100.0/ 0	40	22/ 0	100.0/ 0	22	43/ 0	100.0/ 0	43	152/ 0	100.0/ 0	164
diabetes mellitus	no/ yes	59/0	100.0/ 0	59	40/ 0	97.5/ 2.5	40	22/ 0	100.0/ 0	22	43/ 0	100.0/ 0	43	152/ 0	99.3/ 0.7	164

kidney disease	no/ yes	58/ 1	100.0/ 0	59	39/1	97.5/ 2.5	40	21/ 1	95.5/ 4.5	22	43/ 0	100.0/ 0	43	151/ 1	98.0/ 2.0	164
hyperthyroidism	no/ yes	48/ 11	98.1/ 1.9	59	39/1	87.5/ 12.5	40	19/ 3	86.4/ 13.6	22	43/ 0	100.0/ 0	43	149/ 3	83.6/ 16.4	164
hypothyroidism		59/ 0	79.2/ 20.8	59	35/ 5	100.0/ 0	40	22/ 0	100.0/ 0	22	37/ 6	86.0/ 14.0	43	127/ 25	100.0/ 0	164
parkinson´s disease	no/ yes		100.0/ 0	59	40/ 0		40			22	43/ 0	100.0/ 0	43	152/ 0		164
alzheimer´s disease		59/ 0				100.0/ 0		22/ 0	100.0/ 0						100.0/ 0	
			100.0/ 0	59	40/ 0		40			22	43/ 0	100.0/ 0	43	152/ 0		164
head surgery	no/ yes															
paranasal sinuses	no/ yes	54/ 5				95.0/ 5.0		22/ 0	100.0/ 0						100.0/ 0	
nasal septum	no/ yes	59/ 0	90.2/9.8	59	38/ 2	100.0/ 0	40	22/ 0	100.0/ 0	22	43/ 0	100.0/ 0	43	152/ 0	97.4/ 2.6	164
nasal conches	no/ yes	58/ 1	100.0/ 0	59	40/ 0	97.5/ 2.5	40	20/ 2	100.0/ 0	22	41/ 2	95.3/ 4.7	43	148/ 4	99.3/ .7	164
polyps	no/ yes	59/ 0	98.1/ 1.9	59	39/ 1	97.5/ 2.5	40	20/ 2	90.9/ 9.1	22	43/ 0	100.0/ 0	43	151/ 1	94.7/ 5.3	164
middle ear	no/ yes	57/ 2	100.0/ 0	59	39/1	97.5/ 2.5	40	20/ 2	100.0/ 0	22	40/ 3	93.0/ 7.0	43	144/ 8	99.3/ .7	164
		58/1	96.2/ 3.8	59	39/ 1	100.0/ 0	40	20/ 0	100.0/0	22	43/ 0	100.0/ 0	43	151/ 1	100.0/0	164
Alcohol	yes/ no		98.1/ 1.9	59	40/ 0		40			22	43/0	100.0/ 0	43	152/0		164
Alcohol frequency	rarely/ medium/	27/ 32				45.0/ 55.0		13/ 9	59.1/ 40.9						53.7/ 46.3	
	frequently/ very	22/ 5/ 0/ 0	45.1/ 54.9	59	18/ 22	55.6/ 38.9/	40	6/ 3/ 3/ 1	46.2/ 23.1/	22	29/ 14	67.4/ 32.6	43	80/ 69	64.6/ 24.1/	164
	frequently		82.6/ 17.4/	27	10/ 7/ 1/ 0	5.6/ 0	18		23.1/ 7.7	13	18/ 7/ 3/ 1	62.1/ 24.1/	43	51/ 19/ 7/ 2	8.9/ 2.5	79
current smoking	no/ not anymore /		0/ 0									10.3/ 3.4				
	occasionally/	36/ 16/ 6/ 1				42.5/ 37.5/		17/ 2/ 1/ 2	77.3/ 9.1/		32/ 6/ 4/ 1			102/ 38/	62.8/ 23.0/	
	regularly		60.8/ 27.5/	59	17/ 15/ 8	20.0	40		4.5/ 9.1	22		74.4/ 14.0/	43	20/ 4	12.2/2.3	164
			9.8/ 2.0									9.3/ 2.3				
exposure to	yes/ no										1/ 42					
chemicals		4/55				0/ 100.0		1/ 21	4.5/ 95.5					6/ 164	3.7/96.3	
			7.8/ 92.2	59	0/ 40		40			22		2.3/ 97.7	43			164
preterm birth	yes/ no										6/ 41					
		5/ 54				13.7/ 86.3		2/ 32	5.9/ 94.1					20/ 186	4.1/ 95.9	
knowledge of the	yes/ no		6.8/ 93.2	59	7/ 44		44			34	42/ 5	12.8/ 87.2	47			206
child´s body odour		54/ 5				96.1/3.9		29/ 5	85.3/ 14.7					188/ 18	91.3/ 8.7	
growth of pubic	not begun/ slowly		91.9/ 8.1	59	49/ 2		51			34	1/ 1/ 11/	89.4/ 10.6	47	70/ 3/ 26/	47.3/ 2.0/	206
hair	begun/ definetly	59/ 0/ 0/0				82.6/ 2.2/		12/ 1/ 11/ 10	35.3/ 2.9/		34	2.1/ 2.1/		49	17.6/ 33.1	
	begun/ adult		100/ 0/ 0/ 0	59	38/ 1/ 3/ 4	6.5/ 8.7	45		32.4/ 29.4	19		23.4/ 72.3	47			148
	not begun/ slowly															
breast growth	begun/ definetly										0/ 0/ 7/ 17			26/ 10/ 19/	33.8/ 13.0/	
	begun/ adult	59/ 0/ 0/ 0				60.9/ 21.7/		3/ 4/ 9/ 3	15.8/ 21.1/			0/ 0/ 29.2/		22	24.7/ 28.6	
	not begun/ slowly		100/ 0/ 0/ 0	59	14/ 5/ 2/ 2	8.7/ 8.7	23		47.4/ 15.8	15		70.8	24			77
	begun/ definetly										3/ 5/ 6/ 9					
beard growth	begun/ adult													43/ 6/ 8/ 14	60.6/ 8.5/	
	no/ yes	59/ 0/ 0/ 0				95.7/ 0/ 0/		9/ 1/ 1/ 4	60.0/ 6.7/			13.0/ 21.7/			11.3/ 19.7	
	not begun/ slowly		100/ 0/ 0/ 0	59	22/ 0/ 0/ 1	4.3	23		6.7/ 26.7	19		26.1/ 39.1	23			71
	begun/ definitely										0/ 24			37/ 40		
menstruation	begun/ adult										2/ 3/ 2/ 16			38/ 8/ 3/ 22	48.1/ 51.9	
voice break		59/ 0				82.6/ 17.4		8/ 11	42.1/ 57.9			0/ 100.0			53.5/ 11.3/	
		0/ 0/ 0/ 0	100/0	59	19/ 4	91.3/ 4.3/	23	6/ 3/ 1/ 5	40.0/ 20.0/	19		8.7/ 13.0/	24		4.2/ 31.0	77
			100/ 0/ 0/ 0		21/ 1/ 0/ 1	0/ 4.3	23		6.7/ 33.3	15		8.7/ 69.6	23			71

Supplementary Table 3. *Descriptive values of pleasantness ratings (M, SE, SD, CI) depicted for each BO sample for each age group; and for BOs chosen as "own child" vs. non-chosen as "own child".*

BO	age group	across all BOs				BOs chosen as "own child"				BOs not chosen as "own child"			
		M	*SE*	*SD*	*CI*	*M*	*SE*	*SD*	*CI*	*M*	*SE*	*SD*	*CI*
own child	0-3	64.82	2.89	24.85	[59.07; 70.58]	76.63	4.58	23.79	[67.22; 86.04]	58.04	3.36	23.05	[51.27; 64.81]
	4-8	65.46	3.32	23.91	[58.80; 72.12]	70.39	4.48	18.99	[60.94; 79.83]	62.85	4.46	26.02	[53.77; 71.93]
	9-13	60.40	3.62	23.44	[53.10; 67.71]	66.18	6.20	20.56	[52.37; 79.99]	58.35	4.37	24.36	[49.42; 67.29]
	14-18	65.61	2.97	21.83	[59.65; 71.57]	66.45	4.64	21.75	[56.81; 76.10]	65.03	3.93	22.21	[57.02; 73.04]
	across all	64.43	1.58	23.57	[61.21; 67.45]	60.80	1.89	23.82	[56.87; 64,47]	70.85	2.47	21.79	[65.89; 75.76]
HLA similar same age group	0-3	64.04	2.76	23.95	[58.53; 69.55]	75.45	6.03	20.01	[62.01; 88.90]	62.08	3.02	24.15	[56.04; 68.11]
	4-8	59.65	3.82	27.52	[51.99; 67.32]	54.75	8.56	29.66	[35.91; 73.59]	61.12	4.28	27.07	[52.47; 69.78]
	9-13	61.42	3.93	24.45	[53.45; 69.39]	63.67	12.98	22.48	[7.82; 119.51]	61.23	4.17	24.69	[52.75; 69.71]
	14-18	55.28	3.48	25.34	[48.30; 62.27]	69.50	7.14	17.48	[51.16; 87.84]	53.47	3.75	25.74	[45.91; 61.03]
	across all	60.41	1.71	25.27	[57.03; 63.78]	59.54	1.85	25.34	[55.87;63.20]	65.47	4.35	24.62	[56,59; 74.35]
HLA dissimilar same age group	0-3	57.99	2.75	24.61	[52.52; 58.29]	72.00	4.38	16.39	[62.53; 81.46]	55.02	3.09	25.12	[48.84; 61.19]
	4-8	57.06	3.41	25.08	[50.21; 63.90]	72.62	5.96	16.85	[58.54; 86.71]	54.35	3.75	25.42	[46.80; 61.90]
	9-13	53.38	4.08	24.85	[45.09; 61.66]	56.17	9.21	22.56	[32.49; 79.84]	52.84	4.59	25.58	[43.46; 62.22]
	14-18	59.33	3.01	22.35	[53.28; 65.37]	60.00	6.62	19.85	[44.74; 75.26]	59.20	3.39	23.01	[52.36; 66.03]
	across all	57.33	1.61	24.15	[54.17; 60.50]	55.51	1.79	24.67	[51.97;59.05]	66.65	3.11	18.94	[60.33;72.96]
HLA similar different age group	0-3	56.96	2.23	21.24	[52.52; 61,38]	79.33	10.40	18.01	[34.60; 96.07]	56.19	2.24	21.00	[51.74; 60.64]
	4-8	58.12	3.12	23.16	[51.85; 64.37]	72.33	10.10	24.74	[46.36; 98.30]	56.37	3.23	22.62	[49.87; 62.86]
	9-13	58.45	4.12	26.68	[50.14; 66.77]	64.00	15.53	26.91	[2.84; 93.84]	58.02	4.32	26.97	[49.28; 66.77]
	14-18	54.72	4.45	26.69	[45.69; 63.75]	54.80	14.68	32.83	[14.04; 95.56	54.71	4.71	26.22	[45.09; 64.33]
	across all	57.16	1.57	23.58	[45.05; 60.26]	56.36	1.61	23.25	[53.18;59.54]]	66.96	6.32	26.06	[53.54;80.43]
HLA dissimilar different age group	0-3	57.34	2.57	24.63	[52.24; 62,44]	72.67	5.23	12.82	[59.22; 86.12]	56.27	2.69	24.94	[50.92; 61.62]
	4-8	56.08	3.53	25.24	[48.98; 63.18]	66.40	11.56	25.85	[34.30; 98.50]	54.96	3.72	25.21	[47.47; 62.44]
	9-13	52.32	3.72	24.65	[44.82; 59.81]	69.50	2.18	4.36	[62.56; 76.44]	50.60	3.98	25.20	[42.54; 58.66]
	14-18	49.64	3.86	24.08	[41.83; 57.45]	51.43	12.21	32.29	[21.56; 81.30]	49.25	3.98	22.54	[41.12; 57.38]
	across all	54.57	1.64	24.69	[51.51; 55.33]	53.75	1.72	24.63	[50.35; 57.17]	63.91	4.99	23.41	[53.5; 74.29]

Note. *Abbreviations: BO = body odour*

Bayesian analyses (compare manuscript, method: statistical analyses)

In order to additionally explore the likelihood of our hypotheses, we used Bayesian statistics [1] using JASP software [2]. We included only H1 and the first assumption of H2 for that analysis, as for these hypotheses basic assumptions about the effect sizes are available based on a previous publication [3].

H1: Mothers are able to identify their own child above chance

We performed a Bayesian Binomial test using the identification of own child (yes/no) as the dependent variable:

Based on a previous study [3] we assumed that the identification ability for the choice between three BO samples is at 75%; and rescaled this to our design with a choice between six BO samples, = 37.5%. We, therefore, did not follow the suggestions from Dienes & Mclatchie (2018, [1]) to divide the value by 2, because the result would then equal the chance level (null hypothesis = correct identification of child does not differ from chance level, chance level = 16.67 %). We hence tested evidence for the

alternative hypothesis (correct identification of own child above chance) against 0.375. Additionally, we tested evidence for the null hypothesis against 0.167. We did this for each age group, as listed in the Table below.

Supplementary Table 4. *Bayesian Factor (BF) for own child identification comparing null and alternative hypothesis*.

age group	**test against 0.167**	**test against 0.375**	**results in favor of**
0-3	BF <0.001	BF 6.7	alternative hypothesis
4-8	BF 0.016	BF 6.0	alternative hypothesis
9-13	BF 1.27	BF 2.2	neither alternative nor null hypothesis
14-18	BF <0.001	BF 4.6	alternative hypothesis

The Table shows a Bayesian Factor (BF) below 3 for all groups in comparison to the null hypothesis, indicating that the null hypothesis is not supported in any of the groups. In addition, the BF is higher 3 for all groups except for age group 9-13, indicating that the alternative hypothesis is supported for those groups. For age group 9-13, neither the alternative hypothesis nor the null hypothesis are supported by the Bayesian analyses.

The interpretation of the BF was guided by Dienes & Mclatchie, 2018 [1] who referred to Jeffrey (1998, [4]), in interpreting a BF of >3 as in favor of the alternative hypothesis.

H2: Mothers prefer the BO of their own child over other children

We performed the Bayesian Factor for a one sample t-test using the preference of the own vs. unfamiliar child as the dependent variable. Based on a previous study [3] we assumed that the difference in pleasantness ratings between the own and unfamiliar children´s BO is 1.3 points (pleasantness ratings on a scale ranging from 1 to 10); and rescaled this to our design (pleasantness ratings on a scale ranging from 1 to 100) thereby expecting a difference of 13 points. According to suggestions from Dienes & Mclatchie (2018), we divided this value by 2; thus, we tested against 6.5.

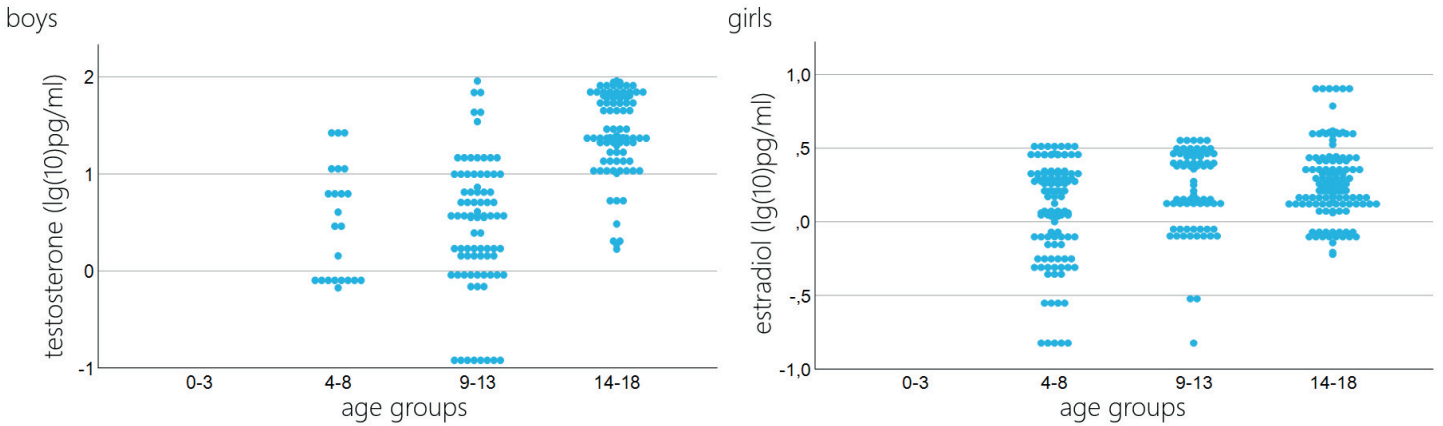
Again, we tested evidence for the alternative hypotheses (significant difference between pleasantness ratings for own vs. unfamiliar children) against 6.5, and additionally, we tested null hypothesis (no difference between own and unfamiliar children) against 0. We performed the analyses for each age group. Results are presented in the Table below.

Supplementary Table 5. *Bayesian Factor (BF) for own child preference comparing null and alternative hypothesis.*

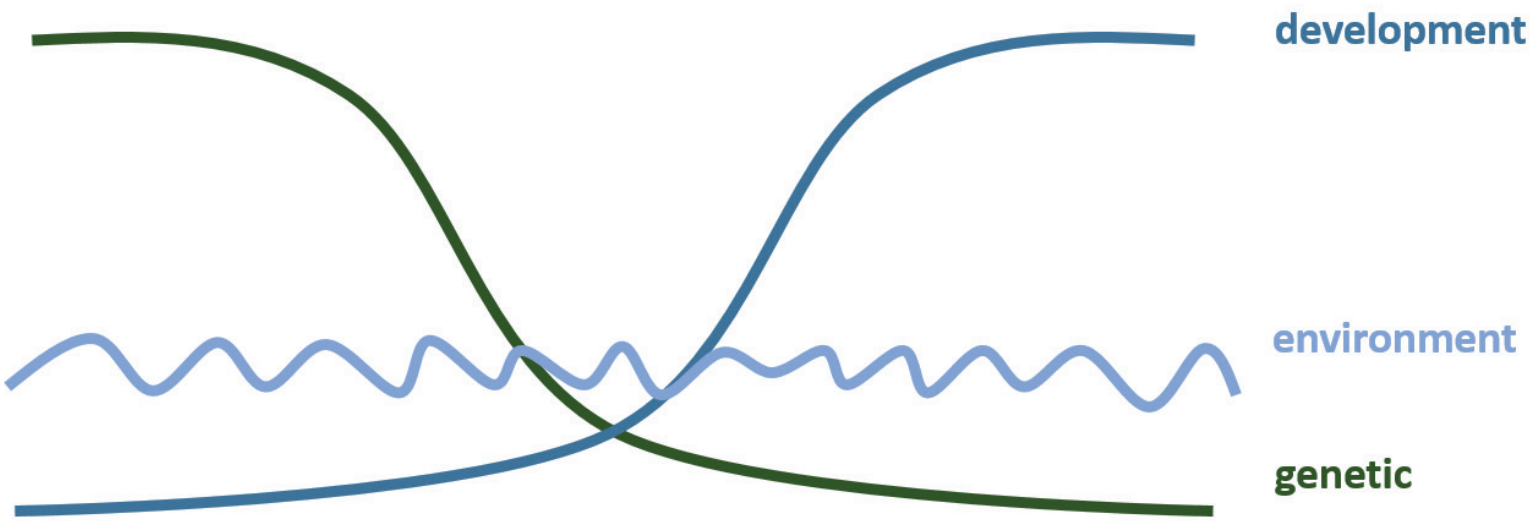
age group	test against 0	test against 6.5	results in favor of
0-3	BF 0.7	BF 7.7	alternative hypothesis
4-8	BF 0.4	BF 5.6	alternative hypothesis
9-13	BF 7.8	BF 2.9	alternative hypothesis rejected
14-18	BF 0.06	BF 3.4	alternative hypothesis

The Table shows a BF below 3 for all groups except of age group 9-13 in comparison to the null hypothesis, indicating that the null hypothesis is not supported for three groups, but supported for 9-13 year old children. In addition, the BF is higher 3 for all groups except for age group 9-13, indicating that the alternative hypothesis is supported for those groups. For age group 9-13 the null hypothesis is supported, meaning that there is no pleasantness preference of the own child´s BO compared to unfamiliar children.

Supplementary figures



Supplementary Figure 1. Hormonal concentration in relation to child´s age group. Hormonal concentration depicted as lg(10), pg/ml. Left: testosterone (boys); right: estradiol (girls).



Supplementary Figure 2. Schematic visualization of factors contributing to maternal pleasantness perception of their child´s BO in relation to age.

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Children's Body Odors: Hints to the Development Status

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Mothers can recognize their own children by body odor. Besides signaling familiarity, children's body odors may provide other information relevant to maternal caregiving behavior, such as the child's developmental status. Thus, we explored whether mothers are able to classify body odors on pre- vs. postpubertal status above chance levels. In total, 164 mothers were presented with body odor samples of their own and four unfamiliar, sex-matched children who varied in age (range 0–18 years). Pubertal status was measured by (a) determining the child's steroid hormone level and (b) parental assessment of the child's developmental stage using the Pubertal Development Scale. Mothers classified developmental status with an accuracy of about 64%. Maternal assessments were biased toward pre-puberty. Classification was predicted by perceptual evaluation of the body odor (i.e. intensity and pleasantness) and by the child's developmental stage, but not by hormones. In specific, mothers with pubertal-aged children classified body odors using the child's developmental status, whereas mothers with younger children only classified body odors using perceptual information (i.e. intensity and pleasantness). Our data suggests that body odors convey developmental cues, but how this developmental information is manifested in body odor remains unclear.

Keywords: olfaction, bonding, puberty, chemosignal, body odors, parent–child relationship, age

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INTRODUCTION

Body odors are a potent chemosignal in human social communication for two reasons. First, they allow recognition of the own relative among a number of individuals (Pause et al., 1998; Lundström et al., 2009). Second, both hedonic [i.e. pleasantness or attractiveness, (Kuukasjärvi et al., 2004; Croy et al., 2017)] ratings and neural activity (Cecchetto et al., 2019) support the idea that body odors communicate affective information to recipients. Both of these features of body odors are highly relevant in the context of mother–child bonding. In specific, kin recognition serves to facilitate a targeted investment of resources (Burnstein et al., 1994; Chapais et al., 2001), which is important for providing one's offspring with care. With regard to the affective value, in a previous study asking for parental perception of their children's body odors, we found that a baby's body odor was perceived as highly adorable and pleasant (Croy et al., 2017). In addition, mothers respond to infant's body odors with neural activation in reward-related processing areas [e.g. neostriate areas (Lundström et al., 2013)]. The authors concluded that the infantile odor may evoke a desire to bond in parents.

Kin recognition has been demonstrated in response to infants, preschool, and adolescent children (Porter et al., 1983; Weisfeld et al., 2003; Ferdenzi et al., 2010). Besides, recognition and

a mother's preference for the body odor of her own child seem to affect each other. For example, mothers who are not able to recognize their own child's body odor do not show a preference for their child's odor. Consistent with this, Croy et al. (2019) showed that mothers with postpartum bonding disorders had a lower preference for their own child's body odor, compared to healthy controls. Further, in a recent study conducted in our lab, we presented 164 healthy mothers to body odor probes of their own and sex-matched unfamiliar children in different age groups, from infancy to adulthood (Schäfer et al., in press). Interestingly, the relationship between source of the body odor (i.e. child vs. other) and odor preference in mothers, varied across the child's development – i.e. mothers preferred their own child's odor when the child was pre- or postpubertal, but not when the child was in early puberty. In that stage, the decrement in maternal pleasantness ratings of their son's body odor was associated with increasing testosterone levels in their sons. In addition, mothers were not able to identify their own child's body odor around puberty but were able to do so in pre- and late pubertal stages. Such findings, led to two suppositions; (1) that the loss of kin recognition with initial hormonal release around puberty is causal for a mother's lack of preference to her child's body odor and (2) that kin recognition and preference of the odor recover over time, because mothers get used to (i.e. are able to identify) the odor again.

In general, developmental cues are necessary for signaling a certain stage of maturity, which affects the amount and the manner of caregiving exerted by parents on their children. Several infantile facial characteristics facilitate a perception of cuteness, and thus elicit approach and attachment behavior (Kringelbach et al., 2016). Those features are lost with increasing development status and in the same time willingness for parental investment declines (Volk et al., 2007). In the domain of olfaction, similar mechanisms may be present.

In order to serve as a developmental cue, it is a prerequisite that body odors change during development. These changes are presumably due to developmental hormones. We base this assumption on the observation that female body odors smell different across the menstrual cycle. In specific, men rate female body odors as more pleasant during ovulation (Havlíček et al., 2017), and this preference is disturbed by women's hormonal contraceptive use (Kuukasjärvi et al., 2004). The particular hormones that mediate this alteration in odor preference across the menstrual cycle are yet to be identified but steroid hormones may be a likely candidate. Steroid hormones seem to affect body odor perception – for example, higher estradiol concentration is associated with higher attractiveness of female body odor (Lobmaier et al., 2018), whereas male body odor contains more androgen-derived steroids and is perceived as more intense (Sergeant, 2010). The relation to actual testosterone levels has however been unclear (Rantala et al., 2006).

As short-term hormonal fluctuations, such as those present during the menstrual cycle, are perceivable via body odor, we also assume that slow, long-term changes of hormonal and pubertal development from infancy (prepubertal stage) to adulthood (postpubertal stage) is reflected in body odor perception. Support for this supposition comes from a questionnaire study asking for parent's evaluation of their children's body odors across development (Croy et al., 2017). Parents reported less pleasantness of odors from their pubertal compared to younger children, which might mirror the increase of steroid hormones during that period.

Puberty is characterized by two main stages of development – the first stage, adrenarche, occurs between the age of 5 and 9 years and is characterized by arise of androgens without leading to visible changes. Children in that phase are still referred to as prepubertal. The second stage, gonadarche, begins between 9 and 11 years and is marked by testosterone and estradiol increase. During that phase, primary and secondary sexual features develop, peaking with transition to adulthood (Dorn et al., 2006).

The present study aimed to address whether body odors function as an indicator for development and explored the ability of mothers to identify a child's developmental stage, using body odor. We hypothesized that mothers are able to accurately distinguish pre- from postpubertal odors (H1). Further, we assumed that this ability depends on developmental familiarity of the mothers: a mother of a prepubertal child might be particularly good at accurately detecting prepubertal status in body odor, whereas a mother of a postpubertal child might be better able to classify postpubertal body odors (H2). Finally, we explored potential mechanisms (maternal perceptual ratings, hormonal and developmental status of the child) contributing to developmental classification of body odor (H3).

MATERIALS AND METHODS

The study was approved by the ethics committee of the University of Dresden (Code: EK 104032015), and all participants provided written, informed consent in accordance with the Declaration of Helsinki. The study was part of a broader project assessing maternal kin recognition and hedonic evaluation of children's body odors (including the dimensions sweetness, wanting, and attraction) in relation to genetic analysis of the human leukocyte antigen complex. In order to facilitate readability, we omit from presenting the whole study here and focus on presentation of parts relevant for the current research question. For all further information, please compare (Schäfer et al., in press).

Participants

The sample consisted of $N = 164$ mothers ($M = 37.5$, $SD = 7.8$) with $N = 226$ children ($M = 7.6$, $SD = 5.9$ years, $n = 124$ girls, $n = 102$ boys), of whom 226 BO probes were sampled. Inclusion criteria was being the biological mother of a child between 0 and 18 years of age. Current pregnancy, insufficient knowledge of German language and anosmia or hyposmia were exclusion criteria. Olfactory performance was assessed prior to study inclusion with a short version of the standardized Sniffin Stick's Step II® screening for olfactory identification ability (Lötsch et al., 2016). In addition, prior to the experiment mothers were asked if they had acute rhino-sinonasal disorders (which could impair olfactory abilities), and were postponed to a later date if they reported having so.

Study Procedure

Participants came to an initial meeting in the lab of the Department of Psychosomatics at the University Hospital Dresden, in which the study procedure was explained and inclusion and exclusion criteria were tested. After meeting those criteria, participants were equipped with a study kit for sampling the body odors and hormonal status of their children at home.

The study kit included odorless shower gel, odorless detergent, a salivette (Salivette®, code blue, SARSTEDT AG & Co. KG, Nümbrecht, Germany), an unworn 100% cotton t-shirt or onesie in the respective size of the child, a re-closeable plastic zip bag, and a study protocol. In order to minimize potential sources of smell, the garment had been washed by the experimenter with an odorless detergent. The protocol contained detailed instructions for body odor and hormonal sampling, and also screened for potential confounders of the body odor sample – i.e. the presence of contamination of the sample (e.g. urine or feces), the medical condition of the child (use of drug and current illness), and the situation at home (smoking, pets, and number of persons who sleep in the children's room).

BO Sampling

The children slept for one night in the garment. Prior to that, parents were instructed to wash sheets and clothes additionally worn to the garment with odorless detergent (Denkmit Vollwaschmittel Ultra Sensitive, dm-drogerie markt GmbH & Co. KG, Karlsruhe, Germany[1]) and the children were asked to shower with the odorless shower gel (both EUBOS flüssig wasch+dusch, Dr. Hobein GmbH, Meckenheim, Germany[2]), as well as to refrain from usage of any perfumed hygiene products. After wearing the garment for one night, the sample was stored in a re-closeable plastic zip bag and brought back to the lab by the parents the next morning, which was where the sample was cut in half and then frozen (−25°C) until the experiment was carried out.

Hormonal Sampling and Assessment of Development Status

For all children aged between 5 and 18 years, hormonal sampling and maternal assessment of the pubertal status using the Pubertal Development Scale [PDS, (Watzlawik, 2009)] was performed. Hormonal sampling was carried out in the evening before the experimental night in order to measure hormonal status in direct relation to the body odor sample. Mothers were instructed to explain their children to chew for 60 s on the salivette until it contained sufficient saliva. Overnight, the salivette was stored in the fridge and the next morning, saliva and body odor sample were taken to the lab where they were frozen at −25°C until analyses. Hormonal analysis was carried out by the Dresden LabService GmbH. For each sample, testosterone and estradiol concentration was determined via immune-assay analyses as follows (Rohleder et al., 2006).

Concentration of alpha-amylase in saliva was measured by an enzyme kinetic method: saliva was processed on a Genesis RSP8/150 liquid handling system (Tecan, Crailsheim, Germany). First, saliva was diluted 1:625 with double-distilled water by the liquid handling system. Twenty microliters of diluted saliva and standard were then transferred into standard transparent 96-well microplates (Roth, Karlsruhe, Germany). Standard was prepared from "Calibrator f.a.s." solution (Roche Diagnostics, Mannheim, Germany) with concentrations of 326, 163, 81.5, 40.75, 20.38, 10.19, and 5.01 U/l alpha-amylase, respectively, and bidest water as zero standard. After that, 80 ml of substrate reagent (α-amylase EPS Sys; Roche Diagnostics, Mannheim, Germany) were pipetted into each well using a multichannel pipette. The microplate containing sample and substrate was then warmed to 37°C by incubation in a water bath for 90 s. Immediately afterward, a first interference measurement was obtained at a wavelength of 405 nm using a standard ELISA reader (Anthos Labtech HT2, Anthos, Krefeld, Germany). The plate was then incubated for another 5 min at 37°C in the water bath, before a second measurement at 405 nm was taken. Increases in absorbance were calculated for unknowns and standards. Increases of absorbance of diluted samples were transformed to alpha-amylase concentrations using a linear regression calculated for each microplate (GraphPad Prism 4.0c for MacOSX, GraphPad Software, San Diego, CA). The intra- and interassay coefficients for amylase were below 9 and 9%,respectively. The detection threshold for the analyzed samples was at 0.3 pg/ml for estradiol and at 1.8 pg/ml for testosterone.

Mothers completed the PDS (Watzlawik, 2009) which is a standardized assessment of pubertal status with sufficient reliability (r = 0.64–0.69) and validity (self- vs. external assessment, r = 0.39 and 0.83) (Watzlawik, 2009). The PDS comprises three questions for each boys and girls (development of body hair, growth of breast/beard, menarche, and voice break) which are summed up to a score indicating pubertal status (ranging from 3 = puberty has not begun) to 12 (development completed). According to the manual (Crockett and Petersen, 1987; Crockett, 1988; Carskadon and Acebo, 1993), the following categories were defined as indicators for the pubertal status of boys: prepubertal (3 points), early pubertal (4 or 5 points), midpubertal (6, 7, or 8 points), late pubertal (9–11 points), and postpubertal (12 points) status. For girls the classification was: prepubertal (2 and no menarche), early pubertal (3 and no menarche), midpubertal (>3 and no menarche), late pubertal (<7 and menarche), and postpubertal (8 and menarche) status.

Experimental Procedure

One and half hours before the experimental session, body odor samples were thawed. Subjects were asked to refrain from eating, drinking coffee, and smoking 1 h prior to the testing, as well as from usage of perfume on the study day. The experimenter refrained from usage of perfume and wore rubber gloves in order to not confound the odor of the samples.

In total, the mothers assessed six body odor samples including the body odor of the own child and four body odor probes of unfamiliar children, as well as an unworn blank probe (previously washed with the odorless detergent) to control for intensity of the body odor samples. The unfamiliar children were matched to the same sex as the own child and two different age groups (two

[1] www.dm.de
[2] www.eubos.de

children of the same age group as the own child, two children of a different developmental group; i.e. a prepubertal age group when the own child was postpubertal, and vice versa).

For body odor presentation, the experimenter instructed the subject to close the eyes during 6 s of smelling in order to focus on the smell and to not be biased by seeing if the sample belonged to a t-shirt or to a onesie. The sample was placed by the experimenter directly under the nose of the participants, with the armpit pad upward. After 6 s, the probe was placed back and the subject had to open her eyes and to rate the body odor.

Prior to the rating procedure, body odors were presented in a test trial without assessment of the probes. This was done in order to anchor the probes for intensity. The six samples were then rated on pleasantness and intensity using visual analogue scale (VAS), ranging from 0 ("not at all") to 100 ("very"). Afterward, mothers rated the age group of the body odor donor. Therefore, the subjects were instructed to choose one of the following categories for each sample: "<1 year," "1–3 years," "4–8 years," "9–13 years," "14–18 years," and ">18 years."

Statistical Analyses

All statistical analyses were performed with IBM SPSS Statistics 25 (IBM Corp, 2017).

For analyses, three age categories [based off Dorn et al. (2006)] were created to indicate the child's developmental status. These were as follow – prepubertal (0–8 years), midpubertal (9–13 years), and postpubertal (≥14 years). This grouping was confirmed by the prior assessed PDS categories. Almost all (126 out of 128, 98.4%) children aged 0–8 years had a PDS score which indicated prepuberty and 50 out of 55 (90.9%) of the children aged 14–18 years had a PDS score which indicated a late or postpubertal stage. We decided to exclude body odor probes of those seven children whose age groups did not align with the PDS for statistical analysis of H1 and H2. We also decided to exclude body odor probes of the $n = 42$ midpubertal children (9–13 years), as this group comprised children of heterogeneous developmental status at the transition between pre- to postpubertal status, and therefore was not suitable to be classified in one consistent stage (see **Table 1**).

This procedure led to a final sample size of 177 body odor probes for analysis of H1 and H2. As each mother rated multiple body odor samples, this resulted in 890 maternal assessments of developmental stage. For analyzing H3, we used the total sample of 226 body odor probes (=1127 assessments).

All analyses were carried out (a) for all children and (b) only for unfamiliar children excluding the own child's body odor sample from analyses. This additional analysis was done in order to not bias performance due to recognition of the own child's odor and thus assuming to know the age. For reasons of clearness, only analyses for all children are presented here. Results regarding the unfamiliar children are listed in the **Supplementary Material**.

Mothers are able to accurately distinguish pre- from post-pubertal odors (H1); classification ability depends on developmental familiarity of the mothers (H2)

We first assessed whether there was a significant difference of maternal classification in children of prepubertal vs. postpubertal stage using χ^2 test. Subsequently, we tested the sensitivity, specificity and accuracy of classification. Therefore, all maternal answers were categorized in one 4-field matrix for each developmental status, and this was based on their accuracy. The four categories are as follow – (1) a true positive (tp) or hit was assigned in case of correct detection of the developmental status, (2) a true negative (tn) was assigned when a mother correctly rejected the developmental status (e.g. not choosing prepubertal for a postpubertal body odor), (3) a false positive (fp) was assigned when a postpubertal sample was rated as prepubertal (or vice versa), and (4) a false negative (fn) was assigned, when a body odor sample was not detected as pre- or postpubertal even though it was pre-/postpubertal. We calculated sensitivity, specificity, and accuracy of the maternal classification for each developmental status. Additionally, we calculated the RATZ-index indicating how much the maternal hit rate increases compared to the chance level [relative increase of the hit rate compared to the random hit rate (Marx and Lenhard, 2010)]. The index can take values between 0 and 1, with values from 0.3 being seen as an improvement to the random rate.

In order to explore the impact of maternal developmental familiarity, we compared for each mother the classification of those body odor samples which had the same developmental status as the own child (developmental familiar classification) to the classification of those body odor samples which had a different developmental status as the own child (developmental unfamiliar classification). Classification performance across the groups was compared using a 4×2 χ^2 test calculator[3].

We tested the influence of hormonal contraceptive use on maternal classification performance, as this has been previously reported to influence olfactory perception (Derntl et al., 2013). On the day of testing, 38.5% of the mothers stated to use hormonal contraception, 54% stated not to use hormonal contraception, and 7.5% did not reply to this question. Comparison between the groups revealed no significant differences between the groups [χ^2 (1) = 5.70, $p = 0.127$], which is why we did not include this in further analyses. We also compared maternal classification performance for boys and girls within each developmental status, and found no significant differences [prepubertal classification: χ^2 (1) = 3.65, $p = 0.057$; postpubertal classification: χ^2 (1) = 0.10, $p = 0.757$]. Therefore, we did not perform any further sex-specific analyses.

Predictors of pre- vs. postpubertal body odor classification (H3)

For H3, logistic regression analyses including bootstrapping ($n = 1000$) were performed with the binary outcome of pre- vs. postpubertal maternal classification as dependent variable.

As predictors we modeled perceptual evaluation of the body odor (pleasantness and intensity) in order to assess the influence of affective perception on the classification. For exploring the influence of developmental cues on body odor classification, the PDS score and hormonal status (comprising the testosterone status for boys and the estradiol status for girls in pg/ml) were

[3]https://www.socscistatistics.com/tests/chisquare2/default2.aspx

TABLE 1 | Frequencies of all presented body odor samples classified by PDS category and age group.

	Age group					
PDS category	**Prepubertal (0–8 years)**	***n* (%) girls**	**Midpubertal (9–13 years)**	***n* (%) girls**	**Postpubertal (14–18 years)**	***n* (%) girls**
Prepubertal	126 (98.4%)	67 (53.2%)	15 (35.7%)	4 (26.7%)	0	0
Early pubertal	2 (1.6%)	2 (100%)	10 (23.8%)	2 (20.0%)	0	0
Midpubertal	0	0	10 (23.8%)	9 (90.0%)	5 (9.4%)	0 (0.0%)
Postpubertal	0	0	7 (16.7%)	4 (57.1%)	50 (90.9%)	35 (70%)

N = 226 children, n = 124 girls, n = 102 boys, n (%) girls = number and percentage of girls within the respective category.

included as further predictors. All predictors were tested in one model using enter method.

All analyses were performed across all children and all mothers and then for developmental familiar samples and developmental unfamiliar samples separately.

RESULTS

Mothers Are Able to Accurately Distinguish Pre- From Post-pubertal Odors (H1)

When presented to body odors of prepubertal children, mothers stated in 71.6% of the cases that those odors were from a prepubertal donor and in 28.17% that these odors were from a postpubertal donor. When presented to body odors of postpubertal children, mothers stated in 58.6% of the cases that those odors were from a prepubertal donor and in turn, mothers stated in 41.4% of the cases that the odors were from a postpubertal donor (see **Figure 1**). The classification of an odor as postpubertal was significantly higher when mothers were presented to postpubertal odors than when they were presented to prepubertal odors [χ^2 (1) = 10.82, $p = 0.001$]. Furthermore, this result reveals that BOs are more frequently rated as originating from a prepubertal than from a postpubertal donor.

The detection of prepubertal odors was performed with an accuracy of 63%. This value exceeds the 50% chance level. However, the RATZ-index of 0.11 is rather low and suggests that mothers do not perform substantially better than chance. Maternal assessments of prepubertal odors had a sensitivity of 72.0% and a specificity of only 38.7%, indicating that maternal assessments tended to accept the classification of a sample as prepubertal [χ^2 (1) = 472.63, $p < 0.001$].

A similar effect was found for postpubertal body odors, which were detected with an accuracy of 64.0% at an RATZ-index of 0.14. Maternal assessments of postpubertal odors had a sensitivity of only 41.4% and a specificity of 71.2%, indicating that maternal assessments tended to reject the classification of a sample as postpubertal.

Classification Ability Depends on Developmental Familiarity of the Mothers (H2)

Separate analyses of developmental familiar samples and developmental unfamiliar samples revealed that mothers were more accurate in classifying body odors of donors at the same developmental status as their own child (see **Supplementary Figures 1, 2**).

Hence, mothers of prepubertal children could identify prepubertal odors with a higher accuracy of 65.2% (RATZ-index = 0.19; sensitivity = 74.4%; specificity = 43.8%) compared to the 60.6% accuracy of mothers having postpubertal children (RATZ-index: 0.04%; sensitivity = 67.7%; specificity = 35.7%). The difference between maternal classification of developmental familiar samples and developmental unfamiliar samples was significant [χ^2 (1) = 9.84, $p = 0.020$].

Similarly, mothers of postpubertal children were more accurate in classification of postpubertal body odors (developmental familiar samples: accuracy = 65.2%; RATZ-index: 0.19; sensitivity = 43.2%; specificity = 73.6%; developmental unfamiliar samples: accuracy = 62.2%; RATZ-index: 0.07%; sensitivity = 37.7%; specificity = 68.1%) and maternal classification differed significantly between both groups [developmental familiar samples vs. developmental unfamiliar samples: χ^2 (1) = 8.95, $p = 0.029$].

Predictors of Pre- vs. Postpubertal BO Classification (H3)

The overall regression model across all mothers was significant [χ^2 (4) = 79.98, $p < 0.001$], revealing that pleasantness ($p < 0.001$), intensity ($p < 0.001$), and pubertal status (PDS score, $p = 0.007$) predicted developmental classification, while hormones did not relate to maternal decision ($p = 0.952$, see **Table 2**). In particular, higher pleasantness predicted prepubertal classification, whereas higher intensity and higher pubertal status were associated with postpubertal classification (see **Figure 1**).

The further regression models testing the respective groups were significant for developmental familiar samples [χ^2 (4) = 38.62, $p < 0.001$] and for developmental unfamiliar samples [χ^2 (4) = 50.29, $p < 0.001$]. For classification of developmental familiar samples, pleasantness, ($p = 0.001$), intensity ($p = 0.001$), and pubertal status ($p = 0.001$) but not hormonal status ($p = 0.706$) predicted developmental classification (see **Table 3**). Higher pleasantness related to prepubertal classification, whereas higher intensity and higher pubertal status were associated with postpubertal classification. For classification of developmental unfamiliar samples, only the perceptual ratings, pleasantness ($p < 0.001$) and intensity ($p = 0.001$), emerged as significant predictors with higher pleasantness predicting pre-, and higher intensity predicting postpubertal classification (see **Table 4** and **Supplementary Figures 1, 2**).

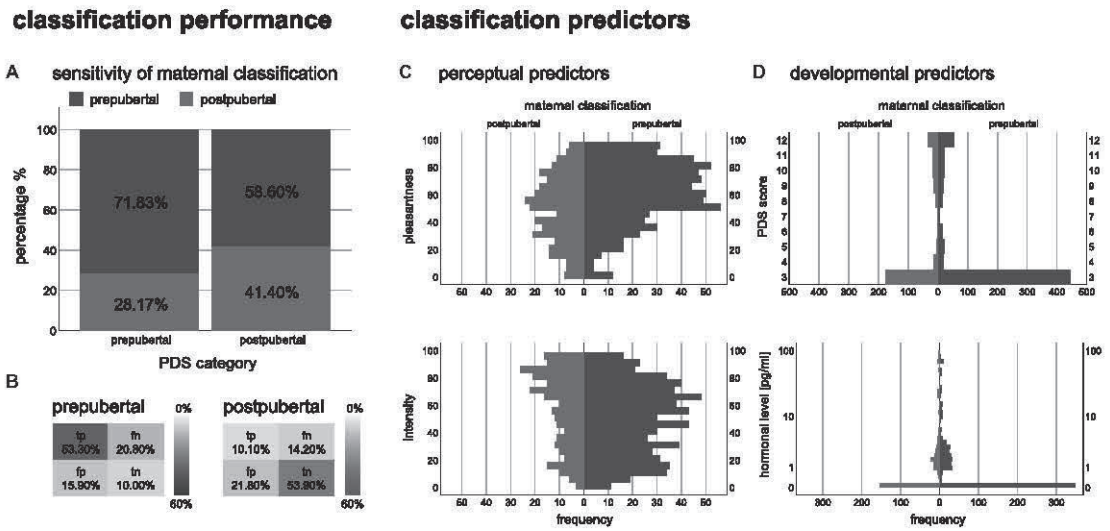

FIGURE 1 | Left panel: classification performance: **(A)** percentage of the sensitivity of maternal classification plotted by PDS categories; **(B)** percentage of frequency of true positives (tp), false positives (fp), false negatives (fn), and true negatives (tn) plotted in blue for prepubertal and in read for postpubertal body odors. Color intensity indicates frequency of choice. Right panel: classification predictors: **(C)** perceptual predictors (above: pleasantness, below: intensity); **(D)** developmental predictors [above: pubertal development scale (PDS), below: hormonal concentration in pg/ml, estradiol for girls, testosterone for boys]. Assessment of developmental predictors was carried out for all children from the age of 5 years on and therefore children under the age of 5 exhibit a value of 3 for the PDS (prepubertal) and a value of 0 for the hormonal concentration.

TABLE 2 | Results of logistic regression model predicting age classification; β, SE, Wald, df, p, e^{β}, 95% CI (e^{β}) of each predictor: all samples.

Predictor	β	SE β	Wald's χ^2	df	p	e^{β}	95% CI (e^{β})	
Pleasantness	−0.018	0.003	34.685	1	0.000	0.982	0.976	0.988
Intensity	0.013	0.003	23.358	1	0.000	1.014	1.008	1.019
Pds	0.062	0.023	7.212	1	0.007	1.064	1.017	1.114
Hormones	0.000	0.005	0.004	1	0.952	1.000	0.989	1.01
Constant	−0.848	0.284	8.928	1	0.003	0.428		

R^2 = 0.08 (Cox and Snell) and 0.12 (Nagelkerke). Model χ^2 (4) = 79.98, $p < 0.001$.

TABLE 3 | Results of logistic regression model predicting age classification; β, SE, Wald, df, p, e^{β}, 95% CI (e^{β}) of each predictor: developmental familiar samples.

Predictors	β	SE β	Wald's χ^2	df	p	Exp (B)	95% CI (e^{β})	
Pleasantness	−0.013	0.004	11.251	1	0.001	0.987	0.979	0.994
Intensity	0.012	0.004	11.426	1	0.001	1.013	1.01	1.02
Pds	0.092	0.028	10.519	1	0.001	1.096	1.04	1.16
Hormones	0.003	0.007	0.142	1	0.706	1.003	0.990	1.02
Constant	−1.240	0.373	11.075	1	0.001	0.289		

R^2 = 0.07 (Cox and Snell) and 0.10 (Nagelkerke). Model χ^2 (4) = 38.62, $p < 0.001$.

DISCUSSION

The present findings highlight that maternal classification of the body odor changes depending on the pubertal stage of the child. Further, accuracy of maternal classification was moderately low (i.e. around 64%). In detail, we observed a high sensitivity and low specificity in detection of prepubertal status and vice versa – i.e. postpubertal classification corresponded to low sensitivity and a high specificity. Hence, mothers were more prone to identify the presented body odors as prepubertal rather than postpubertal.

Mothers performed better when assessing developmental familiar samples than when assessing developmentally unfamiliar samples. This finding may indicate that mothers being exposed to a certain developmental stage are able to incorporate developmental knowledge better. This is illustrated by analysis of the classification's determinants – i.e. perceptual evaluation of the body odor, as well as the assessed pubertal status

TABLE 4 | Results of logistic regression model predicting age classification; β, SE, Wald, df, *p*, e^{β}, 95% CI (e^{β}) of each predictor: developmental unfamiliar samples.

Predictors	β	SE β	Wald's χ^2	df	*p*	Exp (*B*)	95% CI (e^{β})	
Pleasantness	−0.026	0.005	26.491	1	0.000	0.974	0.964	0.994
Intensity	0.014	0.004	10.826	1	0.001	1.014	1.006	1.023
Pds	0.001	0.042	0.000	1	0.990	1.001	0.922	1.086
Hormones	−0.004	0.010	0.182	1	0.670	0.996	0.977	1.015
Constant	−0.160	0.454	0.124	1	0.725	0.852		

R^2 = 0.12 (Cox and Snell) and 0.17 (Nagelkerke). Model χ^2 (4) = 50.29, $p < 0.001$.

predicted the maternal choice. In particular, the developmental familiar classification was guided by perceptual ratings and developmental information, whereas mothers based their decision on perceptual assessment only when rating developmentally unfamiliar samples.

The overall accuracy of developmental classification was low, although exceeding chance level. Body odors consist of various components including rather stable factors, such as the genetic profile (Milinski et al., 2013), but also highly variable influences, such as food, culture (Havlíček et al., 2017), or disease (Olsson et al., 2014). It is unclear how much variance each of these factors explain in odor perception. Typically, odors are difficult to identify in an unaided identification task and susceptible to label effects (Cuevas et al., 2009; Herz, 2003), which explains why odor perception is often ambiguous. Considering those facts, the low odor-identification accuracy found in this study is not surprising. Nonetheless, our data suggest that body odors at least carry the potential to signal developmental stage, which is explained in the following paragraphs.

The maternal susceptibility of detecting prepubertal status suggests that body odors serve as an important signal in human chemical communication. This appears especially true in infancy, when children are dependent on parental care. Parenting in the early childhood is characterized by formation of attachment, enabling the child to survive safely and to develop healthily in the world (Bowlby, 1958). Infantile positive signals, such as a cute baby face or babbling, trigger brain correlates of reward and approach behavior (Kringelbach et al., 2016). This is assumed to apply for body odors as well, and indeed, a baby's body odor elicits reward on a neural level, especially to mothers (Lundström et al., 2013). In our data, prepubertal status was detectable above chance by all mothers, independent from their expert status, which suggests that an infantile body odor may also serve as a universal cue for cuteness, similar to the "Kindchenschema." If this effect were to exist, it might have contributed to the maternal tendency to classify a body odor as prepubertal (rather than postpubertal), observed in this study. Further from an evolutionary perspective, our results may reflect a primacy to interpret children's body odors first as a general "cuteness." We assume that body odor perception leads to neural and behavioral responses similar to those observed for the "Kindchenschema" – i.e. a set of responses targeted to ensure the child's survival by formatting a bond that is prioritized over detachment (Glocker et al., 2009). Preliminary fMRI data from our lab indeed indicate that babies' body odors elicit neural correlates in the maternal brain similar to those reported for facial cuteness (Schäfer et al., 2019). However, further studies investigating the perception of infantile body odors across parents (including fathers) and non-parents still need to clarify the universality of such a stimulus.

Besides cuteness, odors may also communicate a certain degree of maturity. While maternal sensitivity for detecting postpubertal status was lower than for prepubertal status, postpubertal recognition was characterized by a higher specificity. These findings suggest that body odors change with increasing development, – however, which particular features determine this change and drive olfactory perception remains unclear. We did not observe any influence of steroid hormones on age classification. We know from our previous data that steroid hormones can affect maternal evaluation of pleasantness, however this finding is only apparent for male children in the transition from pre-to post-pubertal status [9–13 years (Schäfer et al., in press)].

We did not observe sex-related differences in maternal classification for postpubertal children. However, an important limitation is that we did not assess the menstrual cycle phase of postpubertal girls, which is known to affect body odor assessment (Havlíček et al., 2017). This should be regarded in further studies.

Salivary steroid hormones were measured in this study. These hormones fluctuate across the day (Landman et al., 1976) and do not always relate to secondary sexual features (Shirtcliff et al., 2009). Nevertheless, it is assumed that steroid hormones indicate maturity in the transition phase when the external development is not yet complete (Dorn et al., 2006). Based on our study we cannot exclude that steroid hormones are perceivable in body odor, further studies using different sampling methods may lead to different effects. Here, the external manifestation of pubertal development affected body odor classification, as children of higher pubertal status were more often classified as postpubertal. Further, this effect was driven by the mothers having experience with postpubertal children. As the onset of puberty is complex and characterized by various endocrinological cascades (Grumbach, 2002), we do not know if hormones other than steroids change body odor composition and further promote postpubertal recognition. The need of chemosensory body odor profiling is hence obvious in order to determine volatile odorants, which constitute body odor and affect hedonic evaluation.

As our study points out, perceptual assessment was a strong predictor for age classification across all mothers. Pleasantness was related to prepubertal classification, which is in line with previous findings on positive evaluation of infant's body odor (Fleming et al., 1993; Okamoto et al., 2016; Croy et al., 2017, 2019). Moreover, pleasantness perception of an

infant's odor is an important cue mediating parental care as it facilitates affectionate love (Okamoto et al., 2016). This affective component of body odor declines with age (Okamoto et al., 2016; Croy et al., 2017), which is supported by our results demonstrating that pleasantness drives pre- but not postpubertal classification. The latter was predicted by higher body odor intensity, which has been associated with less positive perception (Doty et al., 1978). In the sense of the mother-child relationship, this leads us to speculate that the intensity drives an avoidant reaction to postpubertal body odors. Hence, this could be interpreted as a mechanism for detachment, when the child becomes more independent and separates itself from parental care (Beyers et al., 2003).

CONCLUSION

In summary, this study demonstrates that developmental information is transcribed in body odor across childhood. While prepubertal status is generally transmitted and characterized by pleasant perception, postpubertal status is rather detected by mothers having expertise with children in that stage, and accompanied by higher intensity ratings. Mothers are further able to encode developmental information for classification when assessing body odors with similar developmental status to their own child. As the composition of body odor is still poorly understood, it remains to be determined how chemicals manifest body odor and how they actually influence olfactory perception.

DATA AVAILABILITY STATEMENT

The datasets generated for this study are available on request to the corresponding author.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Ethikkommission TU Dresden. Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin.

AUTHOR CONTRIBUTIONS

IC, AS, and LS contributed to the conception and design of the study. LS acquired the data and wrote the first draft of the manuscript. LS and IC performed the statistical analysis. IC wrote the sections of the manuscript. AS and KW critically revised the manuscript. All authors contributed to the manuscript revision, and read and approved the submitted version.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpsyg.2020.00320/full#supplementary-material

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Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Supplementary material: Children´s body odors: Hints to the development status

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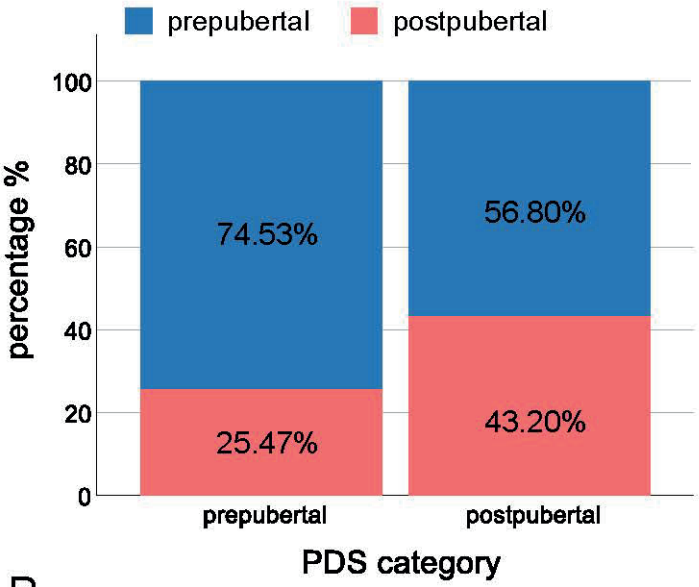
1 Supplementary Figures

developmental familiar samples

classification performance

A sensitivity of maternal classification



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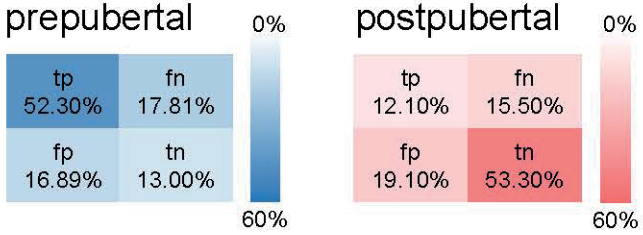
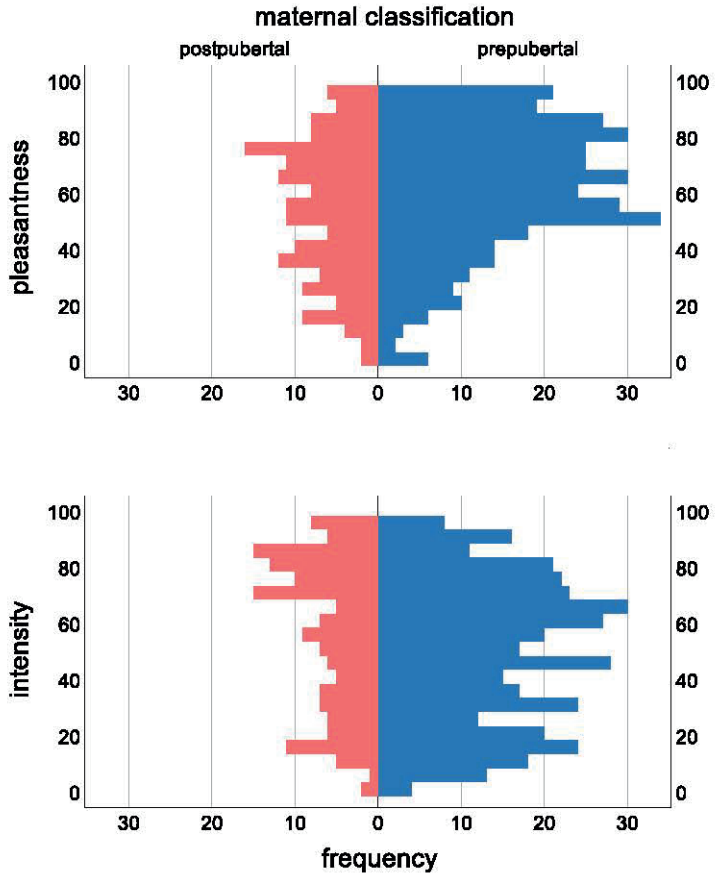


classification predictors

C perceptual predictors



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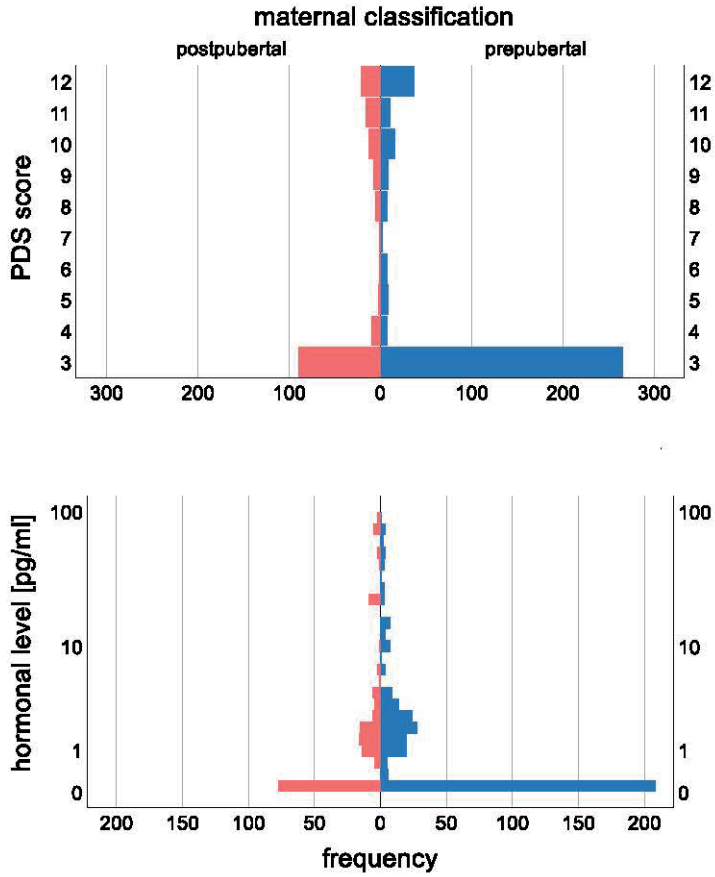
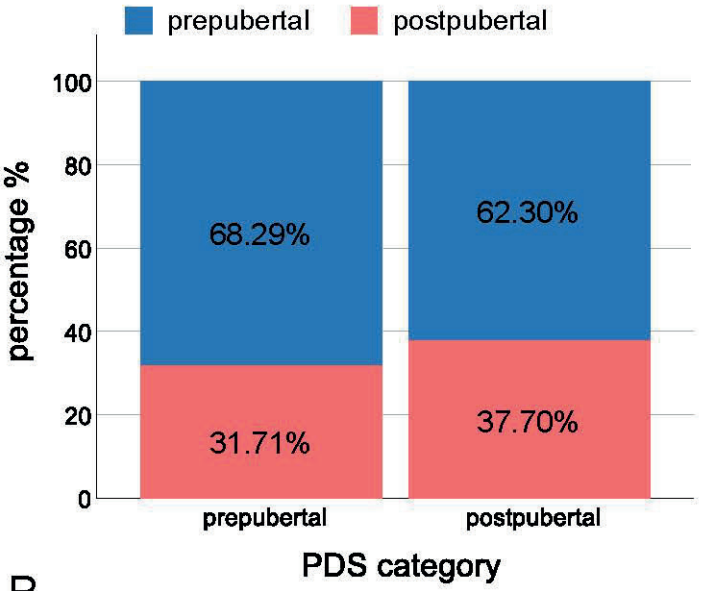


Supplementary Figure 1. Left panel: Classification performance for developmental familiar samples: A: Percentage of the sensitivity of maternal classification plotted by PDS categories; B: Percentage of frequency of true positives (tp), false positives (fp), false negatives (fn) and true negatives (tn) plotted in blue for prepubertal and in read for postpubertal body odors. Color intensity indicates frequency of choice. Right panel: Classification predictors: C: perceptual predictors (above: pleasantness, below: intensity); D: developmental predictors (above: pubertal development scale (PDS), below: hormonal concentration in pg/ml, estradiol for girls, testosterone for boys). Note: Assessment of developmental predictors was carried out for all children from the age of 5 years on and therefore children under the age of 5 exhibit a value of 3 for the PDS (prepubertal) and a value of 0 for the hormonal concentration.

developmental unfamiliar samples

classification performance

A sensitivity of maternal classification



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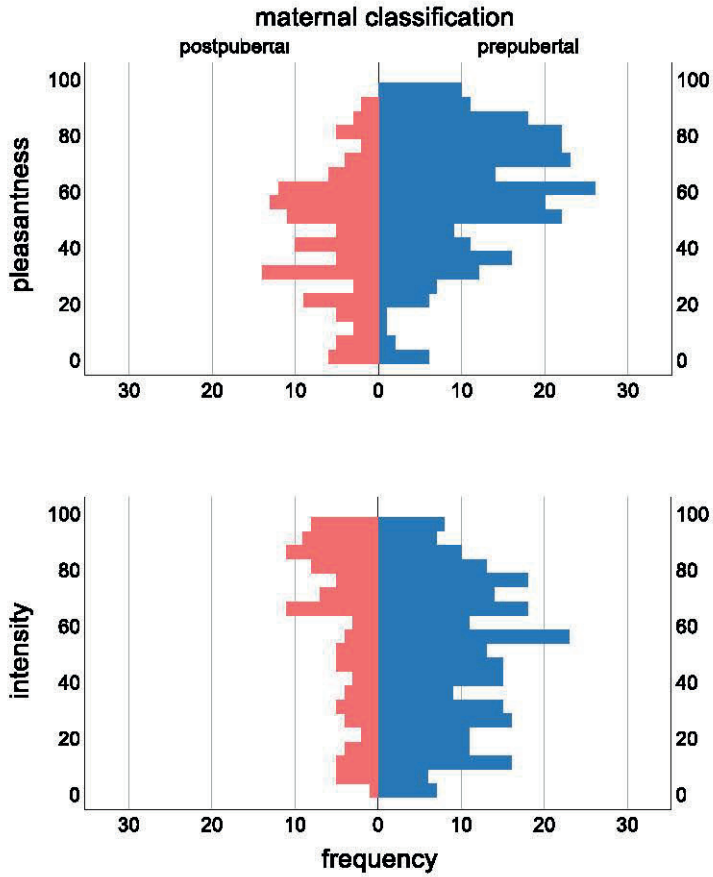
classification predictors

C perceptual predictors



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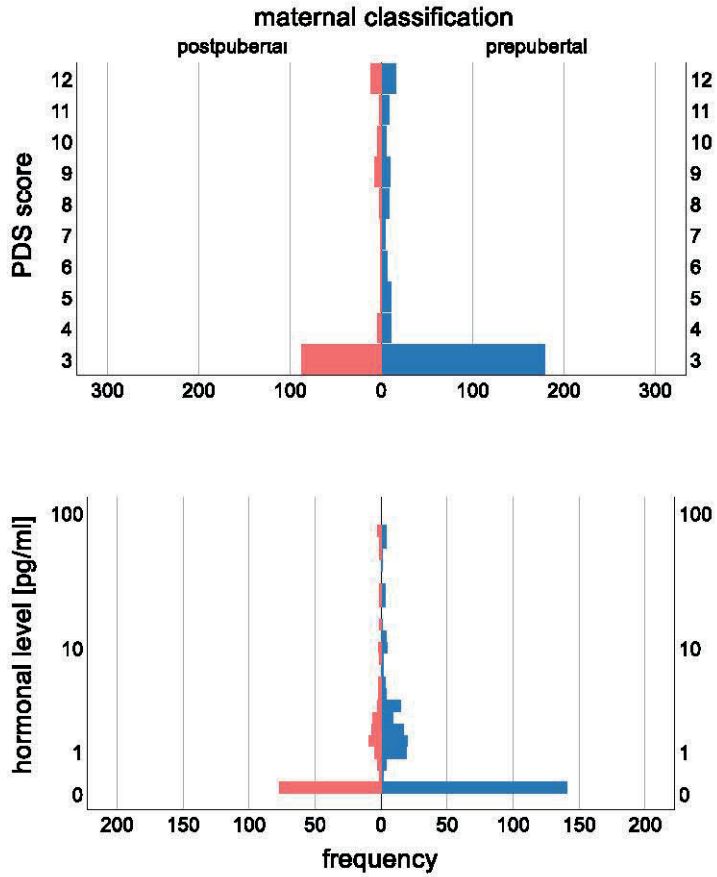


Supplementary Figure 2. Left panel: Classification performance for developmental unfamiliar samples: A: Percentage of the sensitivity of maternal classification plotted by PDS categories; B: Percentage of frequency of true positives (tp), false positives (fp), false negatives (fn) and true negatives (tn) plotted in blue for prepubertal and in read for postpubertal body odors. Color intensity indicates frequency of choice. Right panel: Classification predictors: C: perceptual predictors (above: pleasantness, below: intensity); D: developmental predictors (above: pubertal development scale (PDS), below: hormonal concentration in pg/ml, estradiol for girls, testosterone for boys). Note: Assessment of developmental predictors was carried out for all children from the age of 5 years on and therefore children under the age of 5 exhibit a value of 3 for the PDS (prepubertal) and a value of 0 for the hormonal concentration.

2 Supplementary Results

We explored our hypotheses additionally for all unfamiliar children (excluding the own child´s body odor sample from analyses).

2.1 Mothers are able to accurately distinguish pre- from postpubertal odors (H1)

When presented to body odors of prepubertal children, mothers stated in 69.7% of the cases that those odors were from a prepubertal donor. When presented to body odors of postpubertal children, mothers stated in 62.5% of the cases that those odors were from a prepubertal donor and in turn, mothers stated in 37.5% of the cases that the odors were from a postpubertal donor (compare supplementary Fig. 3). This result indicates that body odor classification towards postpubertal status tended to increase with developmental stage of the child, although this was not significant ($\chi^2(1) = 2.62$, $p = .105$). Furthermore, this result reveals that body odors are more frequently rated as originating from a prepubertal than from a postpubertal donor

Mothers classified prepubertal body odors with an accuracy of 60.8%. This value exceeds the 50% chance level. However, the RATZ-index of 0.07 is rather low and suggests that mothers do not perform substantially better than chance. Maternal assessments of prepubertal odors had a sensitivity of 69.5% at a specificity of only 36.7%, indicating that maternal assessments were biased towards classifying a sample as prepubertal ($\chi^2(1) = 385.83$, $p < .001$).

A similar effect was found for postpubertal BOs, which were detected with an accuracy of 61.9% at an RATZ-index of 0.08. Maternal assessments of postpubertal odors had a sensitivity of only 37.5% and a specificity of 69.5%, indicating that maternal assessments were biased against classifying a sample as postpubertal.

2.2 Classification ability depends on developmental familiarity of the mothers (H2)

Separate analyses of developmental familiar samples and developmental unfamiliar samples revealed that mothers of prepubertal children could identify prepubertal odors with an accuracy of 61.2% (RATZ-index = 0.09; sensitivity = 69.5%; specificity = 35.1%) compared to the 61.8% accuracy of mothers having postpubertal children (RATZ-index: 0.07%; sensitivity = 67.7%; specificity= 35.7%). Classification did not differ significantly between the groups (developmental familiar samples vs. developmental unfamiliar samples: $\chi^2(1) = 5.56$, $p = .135$).

Similarly, both groups did not differ between classification performance of postpubertal body odors (developmental familiar samples: accuracy = 60.2%, RATZ-index: 0.09; sensitivity = 28.4%; specificity = 77.5; developmental unfamiliar samples: accuracy = 60.6%, RATZ-index: 0.07%; sensitivity = 37.7%; specificity = 68.1%; developmental familiar samples vs. developmental unfamiliar samples: $\chi^2(1) = 5.97$, $p = .113$).

2.3 Predictors of pre- vs. postpubertal BO classification (H3)

The overall regression model across all unfamiliar children was significant $\chi^2(4) = 78.40$, $p < .001$. Pleasantness ($p < .001$) and intensity ($p < .001$) significantly predicted age classification with higher pleasantness being associated with prepubertal classification and higher intensity relating to

postpubertal classification. No other predictor contributing to developmental classification was found.

The overall further regression models testing the respective groups were significant for developmental familiar samples ($\chi^2(4) = 50.1$, $p < .001$) and for developmental unfamiliar samples ($\chi^2(4) = 50.28$, $p < .001$). For both groups, perceptual ratings significantly predicted classification: pleasantness (developmental familiar samples: $p < .001$; developmental unfamiliar samples: $p < .001$) with higher pleasantness predicting prepubertal classification, as well as intensity (developmental familiar samples: $p < .001$; developmental unfamiliar samples: $p = .001$), indicating that higher intensity related to postpubertal identification.

Supplementary Tables

Supplementary Table 1. *Results of logistic regression model predicting age classification; β, SE, Wald, df, p, e^{β}, 95% CI (e^{β}) of each predictor: all samples*

Predictor	*β*	*SE β*	*Wald's* χ^2	*df*	*p*	e^{β}	95% CI (e^{β})	
Pleasantness	-.022	.004	39.144	1	.000	.978	.972	.985
Intensity	.016	.003	24.628	1	.000	1.016	1.009	1.022
Pds	.012	.028	.197	1	.657	1.013	.958	1.070
Hormones	-.002	.007	.049	1	.825	.998	.985	1.012
Constant	-.539	.321	2.828	1	.093	.583		

Note. $R^2 = .10$ (Cox & Snell) .14 (Nagelkerke). Model $\chi^2(4) = 78.40$, $p < .001$.

Supplementary Table 2. *Results of logistic regression model predicting age classification; β, SE, Wald, df, p, e^{β}, 95% CI (e^{β}) of each predictor: developmental familiar samples*

Predictors	*β*	*SE β*	*Wald's* χ^2	*df*	*p*	*Exp(B)*	95% CI (e^{β})	
Pleasantness	-.018	.005	13.550	1	.000	.982	.973	.992
Intensity	.016	.005	12.509	1	.000	1.017	1.007	1.026
Pds	.024	.038	.379	1	.538	1.024	.950	1.104
Hormones	.000	.010	.001	1	.975	1.000	.982	1.019
Constant	-.873	.463	3.554	1	.059	.418		

Note. $R^2 = .08$ (Cox & Snell) .12 (Nagelkerke). Model $\chi^2(4) = 50.1$, $p < .001$.

Supplementary Table 3. *Results of logistic regression model predicting age classification; β, SE, Wald, df, p, e^{β}, 95% CI (e^{β}) of each predictor: developmental unfamiliar samples*

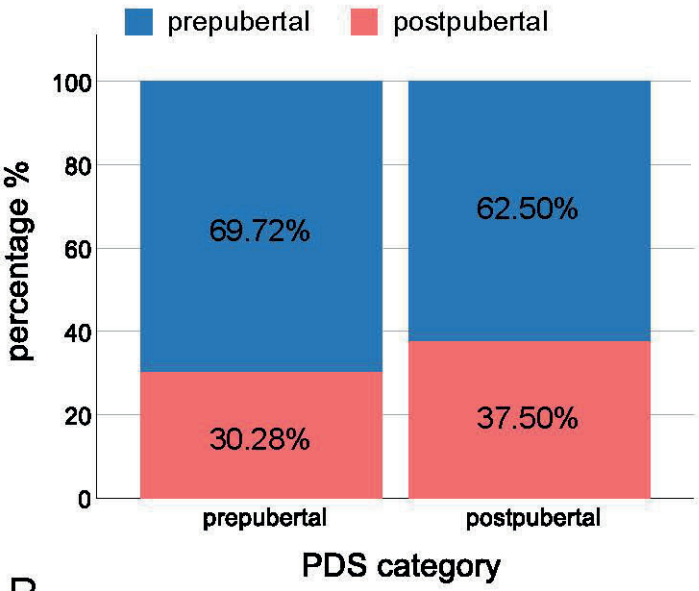
Predictors	*β*	*SE β*	*Wald's* χ^2	*df*	*p*	*Exp(B)*	95% CI (e^{β})	
Pleasantness	-.026	.005	26.491	1	.000	.974	.964	.994
Intensity	.014	.004	10.826	1	.001	1.014	1.006	1.023
Pds	.001	.042	.000	1	.990	1.001	.922	1.086
Hormones	-.004	.010	.182	1	.670	.996	.977	1.015
Constant	-.160	.454	.124	1	.725	.852		

Note. $R^2 = .12$ (Cox & Snell) .14 (Nagelkerke). Model $\chi^2(4) = 50.28$, $p < .001$

unfamiliar children

classification performance

A sensitivity of maternal classification



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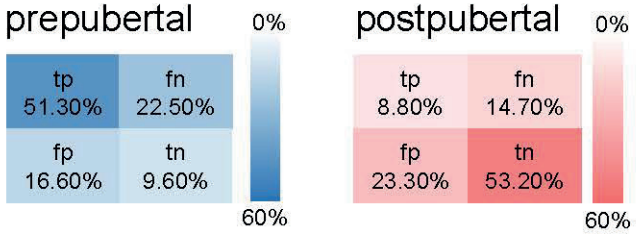
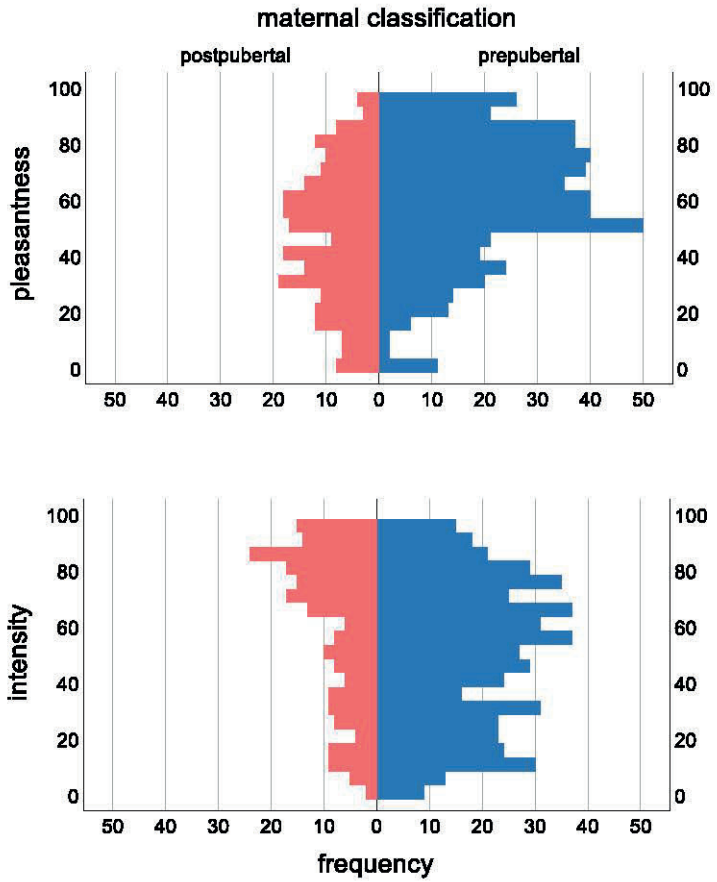
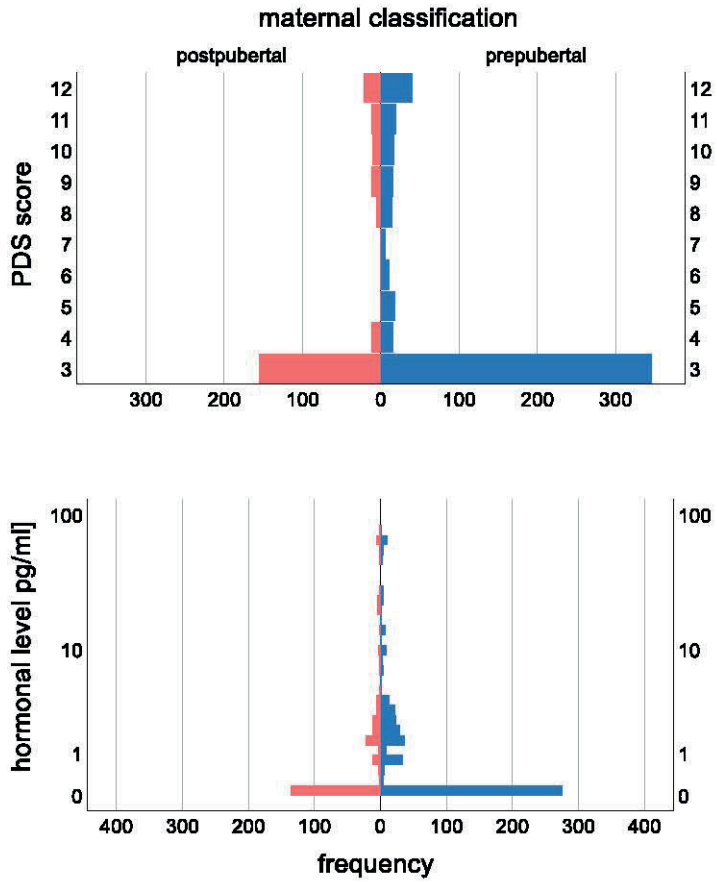


classification predictors

C perceptual predictors



D developmental predictors

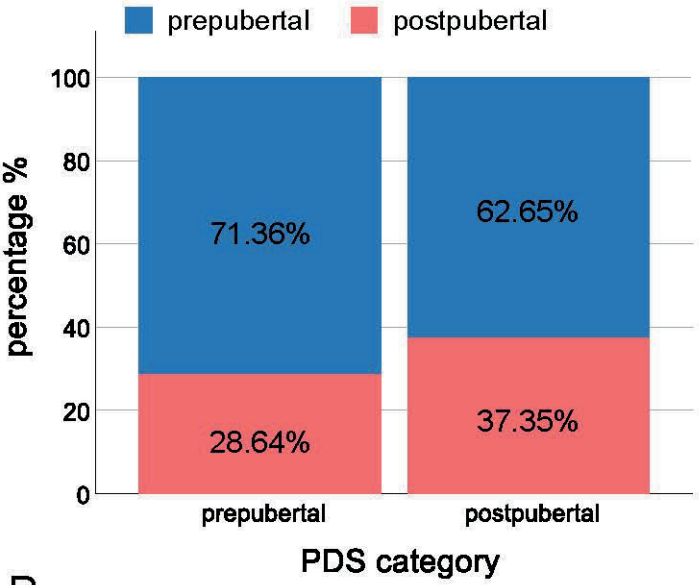


Supplementary Figure 3. Left panel: Classification performance for all unfamiliar children: A: Percentage of the sensitivity of maternal classification plotted by PDS categories; B: Percentage of frequency of true positives (tp), false positives (fp), false negatives (fn) and true negatives (tn) plotted in blue for prepubertal and in read for postpubertal body odors. Color intensity indicates frequency of choice. Right panel: Classification predictors: C: perceptual predictors (above: pleasantness, below: intensity); D: developmental predictors (above: pubertal development scale (PDS), below: hormonal concentration in pg/ml, estradiol for girls, testosterone for boys). Note: Assessment of developmental predictors was carried out for all children from the age of 5 years on and therefore children under the age of 5 exhibit a value of 3 for the PDS (prepubertal) and a value of 0 for the hormonal concentration.

unfamiliar children: developmental familiar samples

classification performance

A sensitivity of maternal classification



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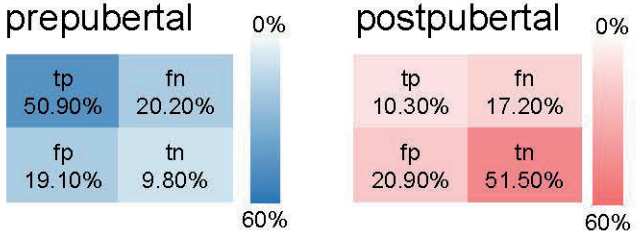

classification predictors

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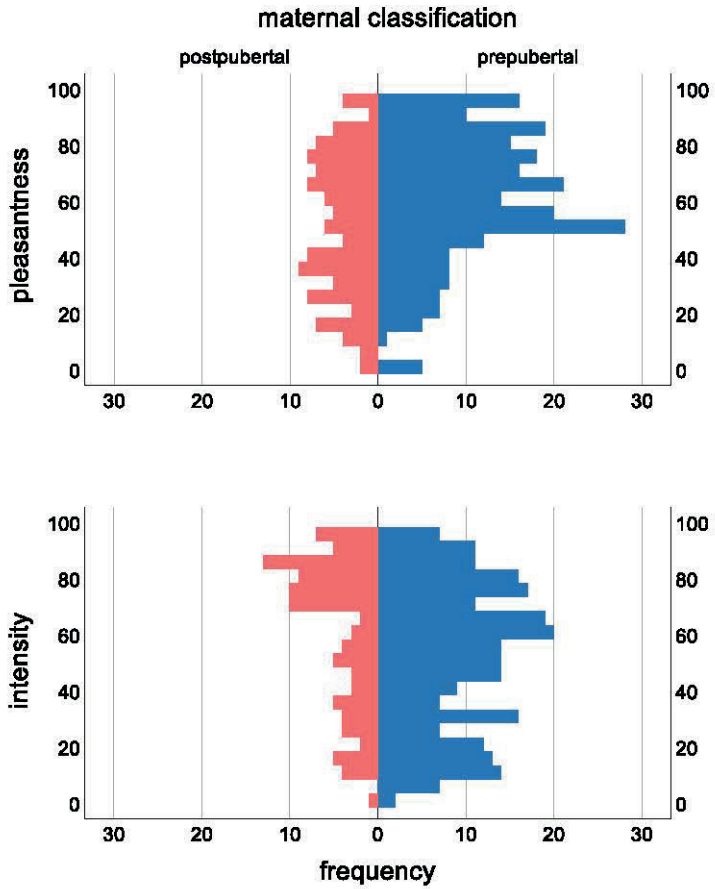
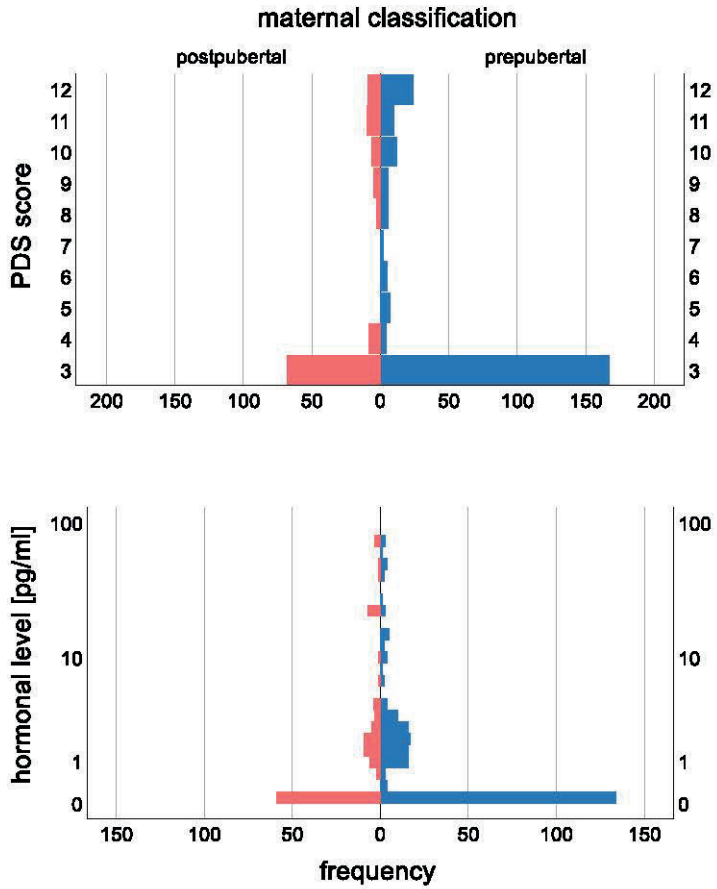


D developmental predictors

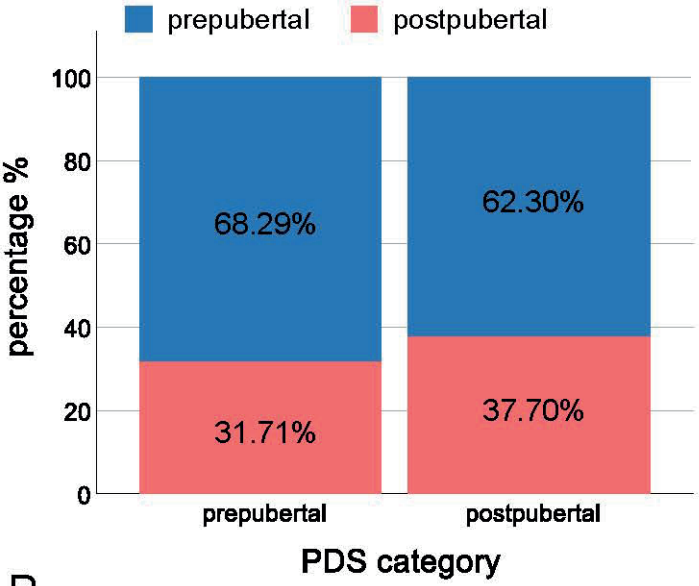


Supplementary Figure 4. Left panel: Classification performance for developmental familiar samples of unfamiliar children: A: Percentage of the sensitivity of maternal classification plotted by PDS categories; B: Percentage of frequency of true positives (tp), false positives (fp), false negatives (fn) and true negatives (tn) plotted in blue for prepubertal and in read for postpubertal body odors. Color intensity indicates frequency of choice. Right panel: Classification predictors: C: perceptual predictors (above: pleasantness, below: intensity); D: developmental predictors (above: pubertal development scale (PDS), below: hormonal concentration in pg/ml, estradiol for girls, testosterone for boys). Note: Assessment of developmental predictors was carried out for all children from the age of 5 years on and therefore children under the age of 5 exhibit a value of 3 for the PDS (prepubertal) and a value of 0 for the hormonal concentration.

unfamiliar children: developmental unfamiliar samples

classification performance

A sensitivity of maternal classification



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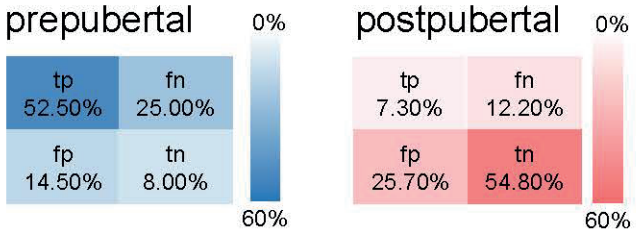
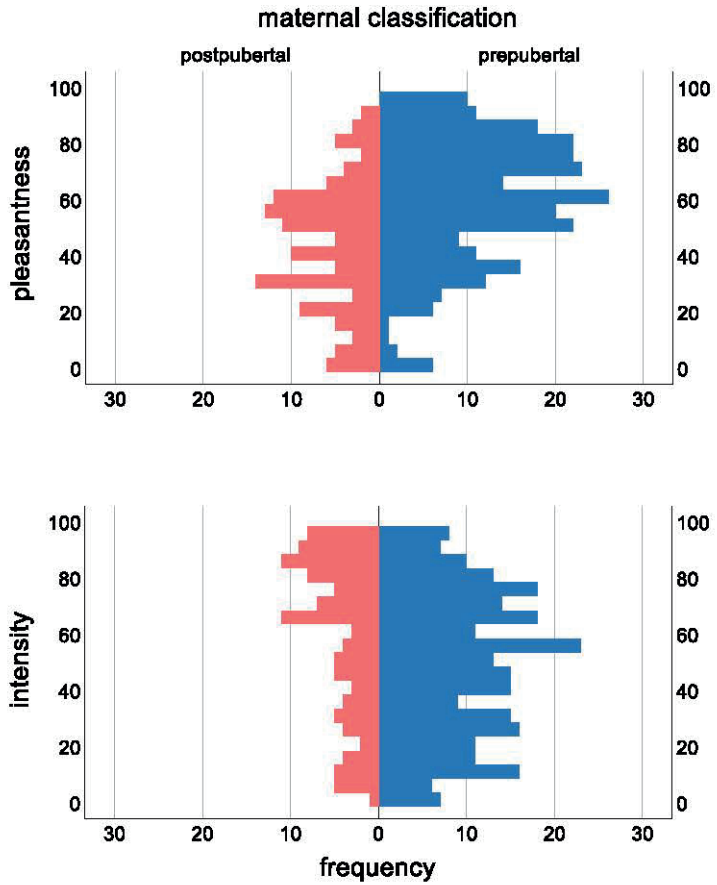
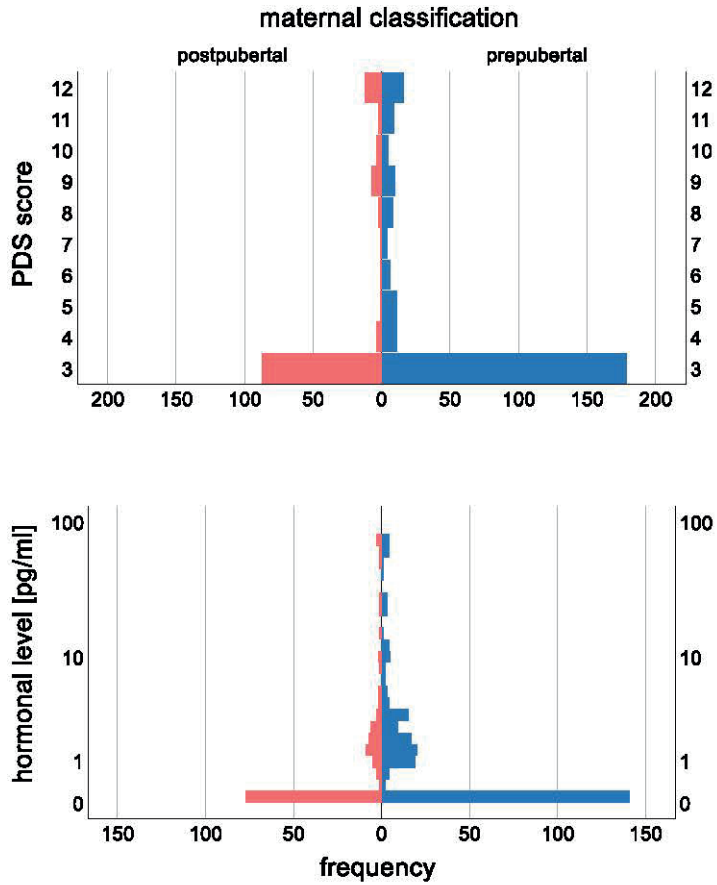


classification predictors

C perceptual predictors



D developmental predictors



Supplementary Figure 5. Left panel: Classification performance for developmental unfamiliar samples of unfamiliar children: A: Percentage of the sensitivity of maternal classification plotted by PDS categories; B: Percentage of frequency of true positives (tp), false positives (fp), false negatives (fn) and true negatives (tn) plotted in blue for prepubertal and in read for postpubertal body odors. Color intensity indicates frequency of choice. Right panel: Classification predictors: C: perceptual predictors (above: pleasantness, below: intensity); D: developmental predictors (above: pubertal development scale (PDS), below: hormonal concentration in pg/ml, estradiol for girls, testosterone for boys). Note: Assessment of developmental predictors was carried out for all children from the age of 5 years on and therefore children under the age of 5 exhibit a value of 3 for the PDS (prepubertal) and a value of 0 for the hormonal concentration.

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The Design Matters: How to Detect Neural Correlates of Baby Body Odors

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Functional magnetic resonance imaging of body odors is challenging due to methodological obstacles of odor presentation in the scanner and low intensity of body odors. Hence, few imaging studies investigated neural responses to body odors. Those differ in design characteristics and have shown varying results. Evidence on central processing of baby body odors has been scarce but might be important in order to detect neural correlates of bonding in mothers. A suitable paradigm for investigating perception of baby body odors has still to be established. We compared neural responses to baby body odors in a new to a conventional block design in a sample of ten normosmic mothers. For the new *short* design, 6 s of continuous odor presentation were followed by 19 s baseline and 13 repetitions were performed. For the conventional *long* design, 15 s of pulsed odor presentation were followed by 30 s of baseline and eight repetitions were performed. Neural responses were observed in brain structures related to basal and higher-order olfactory processing, such as insula, orbitofrontal cortex, and amygdala. Neural responses following the short design were significantly higher in comparison to the long design. This effect was based on higher number of repetitions but affected olfactory areas differently. The BOLD signal in the primary olfactory structures was enhanced by short and continuous stimulation, secondary structures did profit from longer stimulations with many repetitions. The short design is recommended as a suitable paradigm in order to detect neuronal correlates of baby body odors.

Keywords: fMRI design, olfaction, olfactory fMRI, body odor, baby odor, body odor perception

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INTRODUCTION

Neural processing of social stimuli has been well studied for the senses of vision and audition, but examination of interpersonal human chemosensation is just in the beginning due to challenges related to the olfactory system.

The detection of reliable neural activations to odors is complicated due to the anatomical structures of the olfactory system and methodological obstacles related to the presentation of olfactory stimuli (1). We briefly outline those challenges.

Central olfactory processing occurs in several stages [compare (1)]. Olfactory signals coming from the olfactory bulb (OB) pass on to the basal frontal and medial temporal lobe. Thereby, the piriform cortex, the amygdala, the perirhinal and entorhinal cortices receive parts of the incoming information from the OB (2). Those areas are commonly considered as primary olfactory areas (3).

From there, olfactory information is further processed in secondary structures, such as the anterior insula, hippocampus, hypothalamus, and orbitofrontal cortex (OFC). In contrast to other modalities, olfactory processing is characterized by direct pathways projecting into primary and secondary structures without passing through the thalamus first. Due to the subcortical structures involved in olfactory processing, the detection of olfactory signals in functional magnetic resonance imaging (fMRI) is challenging. The olfactory system is surrounded by the frontal and the paranasal sinus, and the acoustic meatus containing various tissues (bones, vessels, air) with different magnetic field homogeneity characteristics (1). Those make this system especially sensitive to susceptibility artifacts and limit signal detection in the mediobasal parts of the brain. Although well-adjusted fMRI sequences can reduce those artifacts, a systematic overview of the most suitable procedures is still missing.

Another difficulty in olfactory fMRI is the odor presentation: stimulus concentration and duration are typically operated by computer-controlled olfactometers, which are stationed outside the scanner and deliver odors via several meters of tubing to the participants' nose. Thus, presenting precise stimulus onsets is challenging. Particular devices, e.g., portable olfactometers, facilitate stimulus presentation, as they allow the odors to be placed close to the MRI scanner or within the scanning room [e.g., (4)].

Besides that, the rapid adaptation to olfactory stimuli needs to be considered (1) and the length of the olfactory stimulation period as neural oscillations occurring after a longer stimulation time may affect the signal (5).

In addition to those general challenges of olfactory fMRI, the stimulation with *body* odors has particular demands: Body odors are generally weak and not easily producible or storable in high concentration as compared to other, e.g., liquid odorants. Typically, clothes worn by the subject serve as body odor stimuli, but the amount of odor molecules within such a piece of clothing is limited. This weaker concentration of molecules may explain the weaker neural activation compared to other olfactory stimuli.

Further, the field of studies investigating neuronal processing of body odors is small and lacks conventions about optimal designs. To our knowledge, only four original fMRI investigations on body odor perception exist (compare **Table 1**). Two used a block design with about 20 s of pulsed odor presentation (6, 7); the other two used an event-related design with about 3 s of continuous odor presentation (8, 9). All four studies report weak activations in general and in some studies the expected olfactory areas were not observed at all. Further studies based on positron emission tomography [PET, (10, 11)], or near infrared spectroscopy [NIRS; (12)] report similar, and again, weak effects (see **Table 1**).

Besides olfactory areas, both the anterior and the posterior cingulate cortex (ACC, PCC) have been associated with body odor perception (6, 10) and it was supposed that the processing of endogenous (body-) odors differs from exogenous odors and activates other brain areas apart from the olfactory system (10).

To our knowledge, only two imaging studies have investigated *baby* body odor perception in mothers [fMRI: (7); NIRS: (12)]. Baby body odors are subtle which implicate that investigations and the detection of strong neural effects are especially challenging. The present study was conducted in order to investigate which design characteristics are particularly suitable for imaging neural responses to baby body odors.

We designed a new, short block presentation paradigm aimed to account for rapid adaptation (by shortening odor presentation time to 6 s) and for weak neural responses following body odors (by increasing the number of stimulus repetitions). We compared this to a long block design, which follows recent recommendations (1) with 15 s of odor presentation; hereby the odor presentation was performed in a pulsed way to overcome adaptation. Our targeted outcome was the strength of neural activation in olfactory relevant brain areas depending on the design. According to previous results, we focused our analysis on the anterior insula, the OFC, the piriform cortex and the thalamus, as well as on the ACC and PCC. We furthermore included the amygdala and the hippocampus as regions of interest (ROI) which are frequently activated in response to odor presentation.

MATERIALS AND METHODS

The ethics committee of the University of Dresden (Code: EK 104032015) approved the conduction of the study according to the "World Medical Association's Declaration of Helsinki." Written, informed consent was obtained from all participants.

Participants

Our sample consisted of 10 healthy, normosmic mothers (aged 27 to 39 years, $M = 32.2$; $SD = 4.7$) having a child under the age of 2 years (aged 10 to 15 months, $M = 10.30$, $SD = 4.22$). Normosmic functioning was ensured with a Sniffin' Sticks identification screening (13). This study was done as a pilot measurement for a larger project.

Magnetic Resonance Imaging Procedures

Functional magnetic resonance data were acquired on a Siemens 3T scanner SONATA with an 8-channel head coil using a protocol with a T2*-weighted gradient-echo, echo-planar imaging sequence ($TR = 2.5$ s, TE 51 ms, flip angle 90°, 25 mm $\times$ 6 mm axial slices, 3.6 $\times$ 3.6 mm in-plane resolution). In order to receive a precise anatomical mapping of the functional data, a high resolution T1 sequence (TR = 2.5 s, 0.7 $\times$ 1mm in-plane resolution) was added. The scanning planes were oriented parallel to the anterior-posterior commissure line and covered olfactory relevant regions from the cerebellum up to the dorsal end of the cingulate cortex. As all areas dorsal to the cingulate cortex were no regions of interest in the present study, we decided to limit the scanned area of axial sections from the brain stem up to the cingulate cortex ($z = 45$ at $y = -80$ to $z = 20$ at $y = 60$) in order to enhance the repetition time and to allow for more scans during the session.

TABLE 1 | Comparison of olfactory imaging studies investigating neural correlates of body odor perception.

	Experimental parameters							Odor presentation			Activation due to odor (vs. baseline)	
Study	***N***	**Design**	**fMRI parameters**	**Number of conditions**	**Repetitions per condition**	**Duration (s); ISI (s)**	**Mode of presentation**	**BO sampling**	**Breathing**	**Airflow**	**Range of *T*-/*Z*-values**	**Results**
Lübke et al. (6)	14 women: high social openness; 12 women: low social openness	fMRI: block design	1.5 T; TR: 2.5 s, TE:40 m; FOV: 192 × 192 mm; matrix: 64 × 64	4 (each 2x male and female BO)	6	22; 22	Pulsed (2 s on, 2 s off)	Axillary sweat	Velopharyngeal closure technique	2l/min	T: 3.71–5.43	BO > BL: SVC: fusiform cortex, ACC, PCC, insula
Lundström et al. (7)	15 women: postpartal;15 women: nulliparous	fMRI: block design	1.5T; TR: 2.63 ms, TE:45 m, FOV: 24 slices axial plane oriented parallel to the planum sphenoidale; matrix: 64 × 64	2 (2x different BO infant)	12	20; 20	Pulsed (1 s on, 4 s off)	Cotton shirts (infants)	Velopharyngeal closure technique	3l/min	Z: 3.64–4.53	BO> BL: hippocampus, insula; SVC: lateral orbitofrontal cortex, putamen, ventral caudate nucleus, dorsal caudate nucleus
McGlone et al. (8)	21 women	fMRI: event-related design	3T; TR:1.5 s, TE:30 ms FOV: 192 × 192 mm; matrix: 64 × 64	2 (pleasant male fragrance; unpleasant artificial BO)	10	2.5; 16.5	Continuous	Artificial BO: thiol compound; male fragrance	Cued breathing (stimulus onset)	4l/min	Z:2.13–2.63	Fragrance < BO: OFC; BO > fragrance: piriform cortex, amygda, frontal operculum, supramarginal gyrus, thalamus
Prehn-Kristensen et al. (9)	28 students: 14 women	fMRI: event-related design	3T; TR:3.25, TE:35 m, FOV: 40 transversal slices covering the whole brain; matrix: 80 × 80	4 (BO anxiety, BO sport; each 2x male and female)	20	3; 17.8	Continuous	Axillary sweat: anxiety and sport condition	Online visual inspection of breathing belt	3l/min	Z: 3.63–5.13	Smelled BO > non-smelled BO: post-central gyrus, medial temporal gyrus, thalamus, putamen, dorsolateral frontal gyrus
Lundström et al. (10)	15 women	PET	–	5 (no odor BL, odor control, BO self, BO friend, BO stranger)	20	3; 5	Continuous	Axillary sweat	Cued breathing (stimulus onset)	–	T: 2.7–4.24	BO > BL and BO > odor control: PCC occipital gyrus, angular gyrus; dorsal medial ACC, angular gyrus
Lundström et al. (11)	12 women: nulliparous	PET	–	4 (no odor BL, odor control, BO sister, BO friend)	20	3; 5	Continuous	Axillary sweat	Cued breathing (stimulus onset)	–	T: 3.5–5	BO > BL: medial cingulate cortex, ACC, superior frontal gyrus, posterior medial frontal gyrus, dorsomedial prefrontal cortex, fronto-temp junction, postcentral gyrus, PCC, angular gyrus, occipital cortex, parietal operculum, insula, culmen
Nishitani et al. (12)	19 women: postpartal; 19 women: nulliparous	NIRS	–	6 (3x different BO infant, 3x unworn cotton shirt)	18	5; 5	Continuous	Cotton shirts (infants)	Cued breathing (stimulus onset)	–	–	BO > BL: PFC activity

fMRI, functional magnet resonance imaging; PET, Positron emission tomography; NIRS, Near infrared spectroscopy; BO, Body odor; FOV, Field of view; BL, baseline; ISI, inter-stimulus interval; s, seconds; min, minute; SVC, small volume corrected; ACC, anterior cingulate cortex; PCC, posterior cingulate cortex; OFC, orbitofrontal cortex; PFC, prefrontal cortex.

TABLE 2 | Mean values and standard deviations for ratings of pleasantness, intensity, and wanting for each design for the single (own, unfamiliar) and merged across own and unfamiliar baby body odor, *T*-Test comparison of the merged (across own and unfamiliar) baby body odor ratings between short and long block design (*t*, df, *p*-value).

	Short block design						Long block design						*t*-test: merged ratings (short vs. long block design)		
Baby odor	**Own**		**Unfamiliar**		**Merged**		**Own**		**Unfamiliar**		**Merged**				
Parameters	***M***	***SD***	***M***	***SD***	***M***	***SD***	***M***	***SD***	***M***	***SD***	***M***	***SD***	***t***	***df***	***p***
Pleasantness	7.30	1.77	6.6	2.01	7.12	1.79	5.70	2.90	6.33	2.34	6.00	2.60	1.97	18	0.065
Intensity	3.70	2.21	4.70	2.91	4.37	2.52	3.40	2.37	4.33	2.87	3.84	2.59	1.06	18	0.304
Wanting	5.70	2.79	5.40	2.91	5.84	2.52	4.20	3.01	6.44	2.12	5.26	2.81	1.07	18	0.300

N = 10; the variables are rated on a 10-point Likert scale; with lower values indicating less and higher values indicating higher pleasantness, intensity, and wanting. When the own baby body odor was presented, two mothers after the short block and one mother after the long block run stated to recognize their own child. When the unfamiliar baby body odor was presented, one mother after the short block and none of the mothers after the long block run stated to recognize their own child. In addition to the comparison reported, we also tested the following contrasts using t-tests for each rating: own (short) vs. unfamiliar (short) and own (long) vs. other (long). No significant differences between the baby odor stimuli were observed.

Body Odor Sampling and Presentation Procedure

Body odor samples were collected with onesies worn for one night by the babies after a standardized procedure (see **Supplementary Material**). The armpit of the onesie was stored in a glass bottle connected with teflon tubes (5 m length) to the air-dilution computer controlled olfactometer (4).

Two different designs of odor presentation were used. Both lasted for the same time of 6 min, but differed in the duration, mode, and number of repetitions of odor presentation within (**Supplementary Figure 1**). This was done in order to match previous design characteristics which used either block designs with long pulsed stimulus presentation (6, 7) or event-related designs with short continuous presentation (8, 9).

Hence, we used a long pulsed block design and compared this to a short odor presentation. The short was similar to previous event-related designs in terms of a short continuous presentation but differed as we did not jitter and randomize the olfactory stimuli within the run. We refrained from that in order to not over complicate the comparison with additional variables as study power was limited.

In the long design, 8 on-blocks of 15-s each in which the odor was delivered were followed each by 8 off-blocks of 30-s each. Due to the long on-blocks, a pulsed odor presentation, where 2 s of air followed every 1 s of odor presentation, was used in order to minimize adaptation and habituation to the odors. In the short design, 13 on-blocks in which the odor was continuously delivered for 6 s were followed each by 13 off-blocks of 19 s each. Each paradigm was tested with two different stimuli in randomized order: the body odor of the own baby and an unfamiliar sex- and age-matched child, resulting in four runs in total. During baseline, clean air was presented. As the main focus of the present study was to compare the design paradigms, the effect of baby body odor was merged across own and unfamiliar baby for statistical analysis. Single results of own and unfamiliar child are provided in **Supplementary Tables 3, 4**. Before the experiment, participants were instructed to breathe regularly through the nose as follows: "You are presented to baby body odors, one of which is your child. Please, breathe regularly and smoothly as normally through the nose." After each run, participants rated pleasantness, intensity, and wanting of the odor stimuli on a Likert-scale ranging from 1 = "not pleasant/intense/not at all" to 10 "very pleasant/intense/very much." Pleasantness and wanting reflect different characteristics of reward (14). Wanting thereby indicates the incentive value of the stimulus and was assessed with the item asking "How much would you like to smell the odor again?," whereas pleasantness displays the hedonic aspect and was assessed by the question "How pleasant is this odor?" In addition, the mothers were asked if the presented odor belonged to their own child ("yes/no/I don't know)." Answers of the behavioral ratings are provided in **Table 2**.

Data Analysis

Data was analyzed with SPM 12 (Wellcome Trust Center for Neuroimaging, London, UK, implemented in Matlab R2014b;

MathWorks, Inc., Natick, MA, USA). The preprocessing was done identically for both designs with the default settings used in SPM 12 and comprised realignment with 2nd degree B-spline, unwarping with 4th degree B-spline, and co-registration by segmentation fitting to the individual T1 volume. The images used for analyses were spatially normalized (stereotactically transformed into MNI ICBM 152-space) and smoothed with a Gaussian kernel of 6 mm FWHM.

For the first level analyses, we started with the two sessions performed with the short design: The full 13 stimulation periods were contrasted to the full ($13 \times 6\,s = 78\,s$) subsequent off-period ($13 \times 19\,s = 247\,s$, compare **Supplementary Figure 1**). We named this contrast "$short_{full}$."

For both sessions performed with the long design, the whole on-period ($8 \times 15\,s = 120\,s$) was contrasted to the whole subsequent off-period ($8 \times 30\,s = 240\,s$). We named this contrast "$long_{full}$."

As the short design comprised more repetitions than the long design, we performed an additional analysis. In order to match the number of repetitions between both designs, we analyzed only the first 8 on- and off–blocks from both sessions. We named this contrast "$short_{reduced}$."

As the long design was characterized by longer stimulus delivery than the short design, an additional analysis was performed. In order to match the stimulation duration, only the first half of the on-period was used ($8 \times 7.5\,s = 60\,s$) and compared to the whole subsequent off-period (compare **Figure 1**). We named this contrast "$long_{reduced}$."

For the second level analyses, four t-contrasts with one-sample *t*-tests were computed for the overall effect of the baby odor (on-period merged across own and unfamiliar baby vs. off period, clean air) for each design and analysis approach ($short_{full}$, $long_{full}$, $short_{reduced}$, $long_{reduced}$) in order to detect general activations related to the odor presentation across all subjects.

As the main aim of this study was not the determination of neural activations, but the exploration of the best suitable design characteristics, the comparison between both designs was based on the signal strength within a given ROI. ROI analyses were performed for the following regions: Anterior insula, OFC, amygdala, hippocampus, ACC, PCC, piriform cortex, and thalamus. ROIs were built with WFU Pick Atlas 3.0.3 (15) toolbox for SPM (for details, see **Supplementary Material**). ROI analyses were performed contrasting the effect of the baby body odor to the baseline condition. For each ROI in each design (apart from the ACC and the piriform cortex where no supra threshold activations were observed), the mean beta signal across all subjects was extracted for a 4 mm sphere around the peak voxel using MarsBar (16).

Subsequently, a generalized linear mixed model (GLM) was performed (IBM SPSS Statistics 25) in order to test the effect of the design on the signal strength. Each participant ($n = 10$) served as an individual, each stimulus (own and other baby) and each ROI (anterior insula, OFC, amygdala, hippocampus, PCC, thalamus) served as repeated measurement. The extracted mean beta signal was used as target for the main effect of the design across all ROIs.

We contrasted the new to the conventional design ($short_{full}$ vs. $long_{full}$). Afterwards, we systematically compared the different analysis approaches to each other in order to specify whether this effect was based on the number of repetitions, duration (length of stimulation period) or mode (continuous or pulsed stimulation) of the presentation. For effect sizes, we calculated Cohen's d. Results within the ROIs are descriptively reported.

In order to explore additional activations following baby odor stimulation, a whole-brain analysis was performed for the strongest design ($short_{full}$). The effect of baby body odor (merged across own and unfamiliar baby) was contrasted to the baseline with a threshold of $p < 0.001$ (uncorrected) and a cluster extent threshold of $k > 20$ (**Supplementary Table 2**, **Supplementary Figure 1**). Analyses of the single effects of each baby body odor (own baby vs. baseline; unfamiliar baby vs. baseline) are presented in the **Supplementary Material** (compare **Supplementary Tables 3, 4**, **Supplementary Figure 2**).

RESULTS

ROI Analyses

There were superior BOLD signal activations in the short design compared to the long design across all ROIs [$short_{full}$ vs. $long_{full}$: $F_{(1,22)} = 8.67$, $p = 0.007$, $d = 0.34$, see **Figure 1**]. We aimed to systematically compare whether this effect was based on number of repetitions, duration, or mode of presentation.

The comparison between the $long_{full}$ to the $short_{reduced}$ design indicated an effect of the number of repetitions: When both designs had the same number of repetitions, the short was not superior to the long design anymore [$F_{(1, 13)} = 1.74$, $p = 0.220$). The comparison of the $short_{full}$ to the $long_{reduced}$ design indicated no effect of stimulation duration: When both designs had the same duration, the short was still superior to the long design [$short_{full}$ vs. $long_{reduced}$: $F_{(1, 159)} = 15.61$, $p < 0.001$, $d = 0.24$).

Thus, the observed superiority of the short design could be either due to *number of repetitions* or to the *mode* of presentation. In order to explore this further, we statistically compared the designs changing the parameter of interest (number of repetitions, mode, duration) and keeping the other two elements constant:

The direct comparison of number of repetitions, when keeping duration and mode constant, did not show a significant effect across the ROIs [$short_{full}$ vs. $short_{reduced}$: $F_{(1, 18)} = 0.01$, $p = 0.922$]. Visual inspection revealed a differential effect: A high number of repetitions led to lower BOLD signal in amygdala and hippocampus, but to higher signal in secondary structures, namely the OFC and PCC (**Figure 1**).

The direct comparison of *mode* when keeping number of repetitions and duration constant, did not show a significant effect across all ROIs [$short_{reduced}$ vs. $long_{reduced}$: $F_{(1, 21)} = 1.59$, $p = 0.221$]. Visual inspections showed a more differential effect, so that continuous presentation led to a higher signal in all ROIs except for the PCC and the anterior insula (**Figure 1**).

The direct comparison of *duration* when keeping number of repetitions and mode constant, did not show a significant effect across the ROIs [$long_{full}$ vs. $long_{reduced}$: $F_{(1, 41)} = 0.67$, $p = 0.419$].

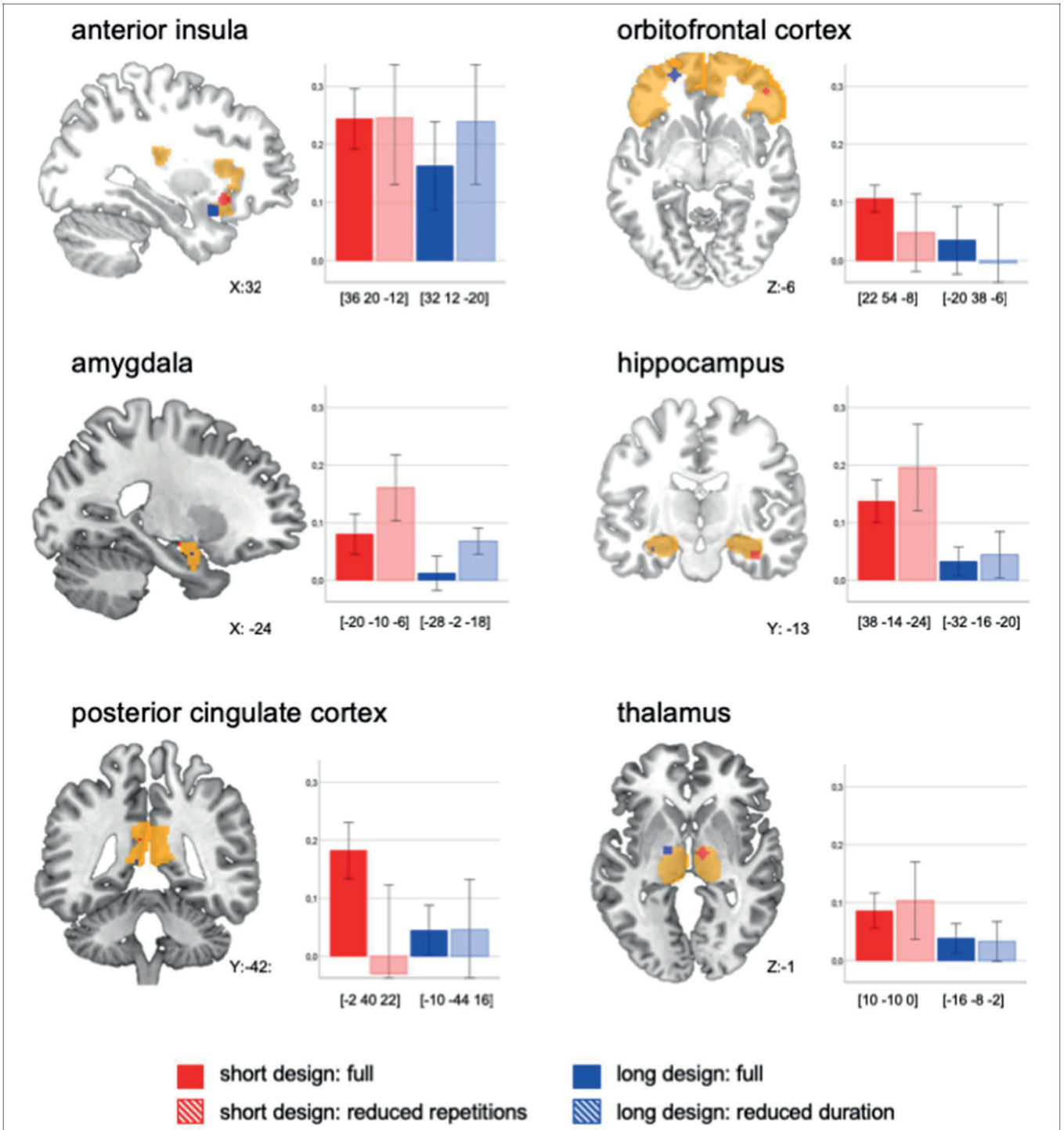

FIGURE 1 | Peak activations displayed for each ROI and each design. Beta mean values (baby body odor vs. baseline) extracted for a 4 mm sphere around the peak value (RH, right hemisphere; LH, left hemisphere, and MNI coordinates are displayed in square brackets) of each ROI and for each design across all subjects ($n = 10$). Please note in the anatomical visualization, that peak activations may have occurred on different hemispheres. Error bars display 95% CI.

Visual inspection showed—again—a more differential effect: a reduced duration of stimulation led to higher signal in amygdala, hippocampus and anterior insula, but to lower signal in the OFC (**Figure 1**).

Whole Brain Analyses

Whole brain analysis was performed for the paradigm with the strongest neural activation ($short_{full}$) and revealed rather weak responses in a total of four significantly activated areas, namely

the superior temporal gyrus (STG), the OFC, the brain stem, and the anterior insula (compare **Supplementary Table 1**).

DISCUSSION

Our results demonstrated superior activations in the short compared to the long design across ROIs. Systematic analyses revealed differential effects on olfactory areas depending on number of repetitions, duration, and mode of the stimulation. The clearest results were observed for the amygdala: for this structure, considered as part of the primary olfactory cortex (3), it seems beneficial to design body odor stimulation with fewer repetitions per run, shorter duration, and continuous presentation. We assume that this effect is due to the rapid habituation and adaptation in primary olfactory areas (17). To overcome the early habituation and preserve power, we suggest a higher number of short runs. Alternatively, stimulation with long and jittered inter-stimulus intervals can be recommended, though this will increase the total duration of the design.

For subsequent and later habituating structures, namely the OFC, many repetitions and long stimulation seem to be beneficial. Such an approach was implemented in the long design. However, great care has to be exerted in order to achieve a sufficient number of repetitions with this design. An optimal combination of long stimulation and high number of repetitions should be weighed. Based on our data we suggest 15 s of stimulation and at least 13 repetitions.

Taken together, our study showed diverse effects on different brain areas. A reduced stimulation duration for instance led to stronger signal in amygdala, hippocampus, and anterior insula, but to weaker signal in the OFC. This matches previous research showing that BOLD signal of hippocampus and anterior insula have similar time courses, while the BOLD signal time course of the OFC is delayed (17). The authors attributed this to the high interconnections, which result in similar patterns between the former structures. The OFC receives likewise direct input from primary olfactory areas (3). Additional incoming information via the thalamic pathway may explain its prolonged response (17). Hence, particular design characteristics should be considered with regard to the areas of interest.

A recent study (5) suggested a benefit of a high number of repetitions and short stimulation duration due to oscillations in the neural signal, which only occur after longer duration. Our study partly supports this assumption, as the combination of short and continuous stimulation with higher number of repetitions showed strongest activations. Yet, this effect could not be linked to the short duration, but rather to differential effects on primary or secondary structures depending on the respective combination of design characteristics.

The comparison in our study refers only to a *block* design. The short design was in fact similar to an event-related design in terms of short continuous stimulation alternating with rather long off-periods (8, 9). However, the stimuli were not randomized within a run; the stimulation was longer than in conventional event-related designs and on-off-periods alternated in the same interval. Further research comparing the short with a randomized and jittered design might be informative.

We are aware that the explanatory power of the study is limited due to the small sample size. However, we like to briefly review the additional results. Beyond the olfactory regions, presentation of baby body odors activated the PCC, as well as the STG. The PCC has been related to social chemosignaling (10), which matches our findings. As the STG is important for social cognition (18), the observed activation in our study might be referred to the social relevance of the baby odor stimuli.

The smell of the own baby is crucial for mother-child interactions and facilitates kin recognition and bonding in many species. In humans, higher reward-associated neural responses to baby body odors were observed in mothers compared to non-mothers (7) and it was suggested that maternal bonding is moderated by olfactory cues. The present study aimed to work out a suitable design for the detection of neural correlates to baby body odors. It provides the ground to examine the differences of neural processing of body odors from the own vs. other children.

CONCLUSION

There is no common paradigm for the detection of neural correlates to body odor perception and the few studies performed in this area showed diverse results. The present study was conducted in order to find optimized design paradigms for presenting baby body odors in the fMRI and results may transfer to general body odor perception. As the short design revealed superior activations, we recommend this as a time-efficient and effective paradigm.

AUTHOR CONTRIBUTIONS

IC, TH, and LS contributed to conception and design of the study. LS acquired the data. LS and IC performed the statistical analysis. LS wrote the first draft of the manuscript. IC wrote sections of the manuscript and TH critically revised the manuscript. All authors contributed to manuscript revision, read and approved the submitted version.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fneur.2018.01182/full#supplementary-material

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Conflict of Interest Statement: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary Material

The design matters: How to detect neural correlates of baby body odors

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1 Supplementary Figures and Tables

Supplementary Table 1

Detailed Overview of the ROI Masks: Atlas, Working Region and Volume of each ROI

ROI	Atlas	Working region	Total volume for bilateral ROIs (mm)
OFC	Ibaspm 116	frontal_sup_orb_L; frontal_sup_orb_R; frontal_mid_orb_l; frontal_mid_orb_r; frontal_inf_orb_l; frontal_inf_orb_r; frontal_mid_orb_l; frontal_mid_orb_r	70680
Insula	Ibaspm 116	insula_L; insula_R	29024
Hippocampus	Ibaspm 116	Hippocampus_L; Hippocampus_R	15024
Amygdala	AAL	Amygdala_L, Amygdala_R	3744
Thalamus	Ibaspm 116	Thalamus_L; Thalamus_R	17256
ACC	Ibaspm 116	cingulum_ant_L; cingulum_ant_R	21704
PCC	Ibaspm 116	cingulum_post_L; cingulum_post_R	6384
Piriform cortex		Piriform cortex L and R built in MRIcron [McCausland Center for Brain Imaging, https://www.mccauslandcenter.sc.edu/crnl/mricron] as guided by [1]	368

Note. All masks except for the Piriform cortex were built with WFU Pick Atlas 3.0.3 [2, 3] toolbox for SPM.

Supplementary Material

Supplementary Table 2

Whole Brain Analysis for Short Block Design: Main Effects of Baby Body Odor (Merged across Own and Unfamiliar Baby), Peak Height Threshold: p<.001, Cluster Extent Threshold: k>20

		Coordinates					
Side	Area	X	Y	Z	Z-Value	T-Value	P_{uncorr}
Odor > No Odor							
Right	STG	68	-30	-6	4.19	5.56	0.000
Right	Brain Stem, allocated to the trigeminal main sensory nucleus, guided by [4]	2	-30	-18	4.01	5.19	0.000
Right	OFC	46	40	-5	3.88	4.94	0.000
Right	Anterior Insula	36	16	-7	3.87	4.92	0.000

Supplementary Table 3

Whole Brain Analysis for Short Block Design: Main Effect of Own Baby Body Odor, Peak Height Threshold: p<.001, Cluster Extent Threshold: k>20

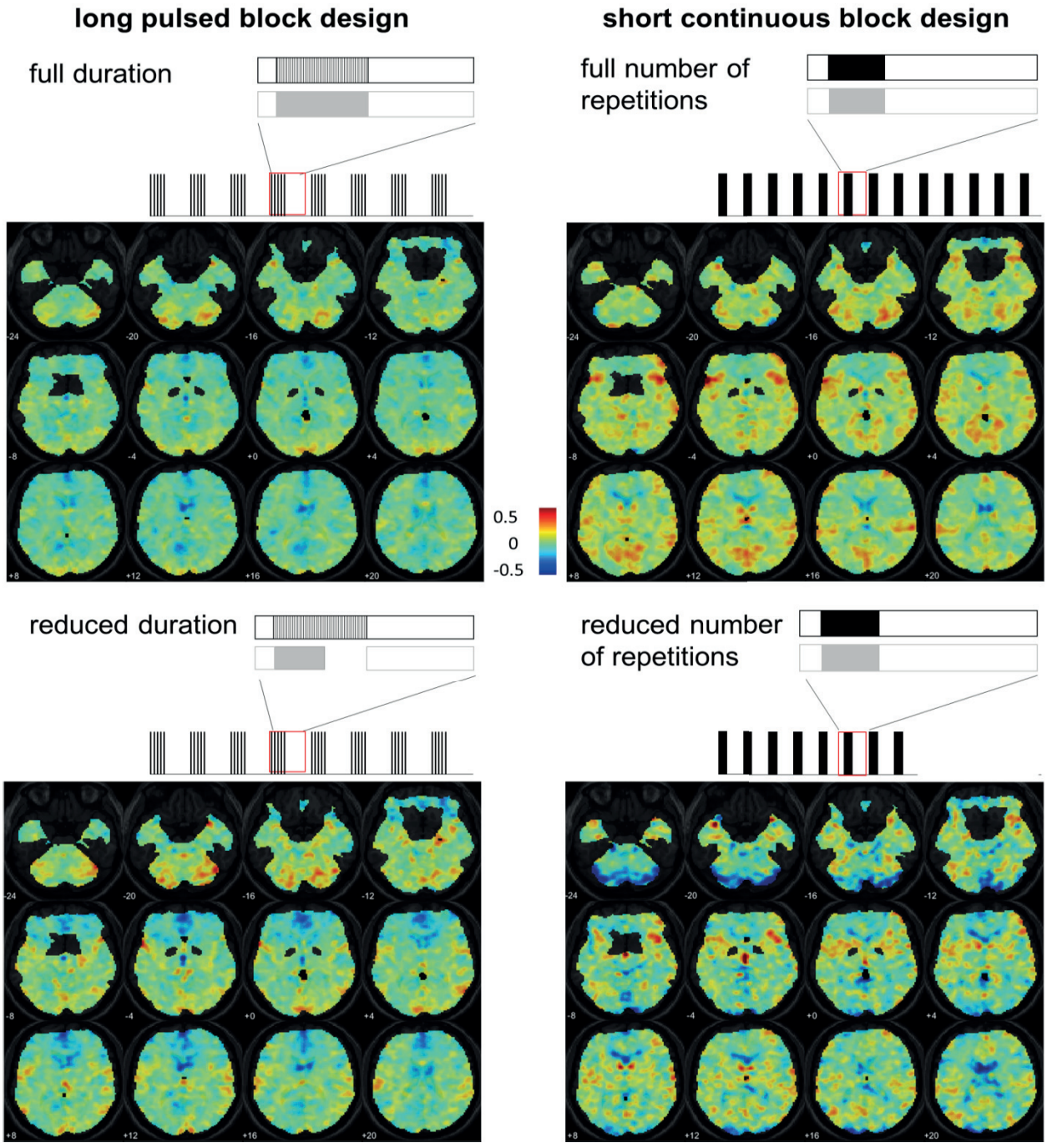
		Coordinates					
Side	Area	X	Y	Z	Z-Value	T-Value	P_{uncorr}
Own > No Odor							
Right	Mediate Cingulate Cortex	10	-32	30	4.14	5.46	0.000
Right	OFC	44	44	-10	3.61	4.46	0.000
Left	PCC	-2	-42	22	3.95	5.08	0.000
Left	Parahippocampal Gyrus / Subiculum	-18	-34	-12	3.88	4.95	0.000

Supplementary Table 4

Whole Brain Analysis for Short Block Design: Main Effects of Unfamiliar Baby Body Odor, Peak Height Threshold: p<.001, Cluster Extent Threshold: k>20

		Coordinates					
Side	Area	X	Y	Z	Z-Value	T-Value	P_{uncorr}
Unfamiliar > No Odor							
Left	Parahippocampal Gyrus/Subiculum	-8	-28	-14		5.26	0.000

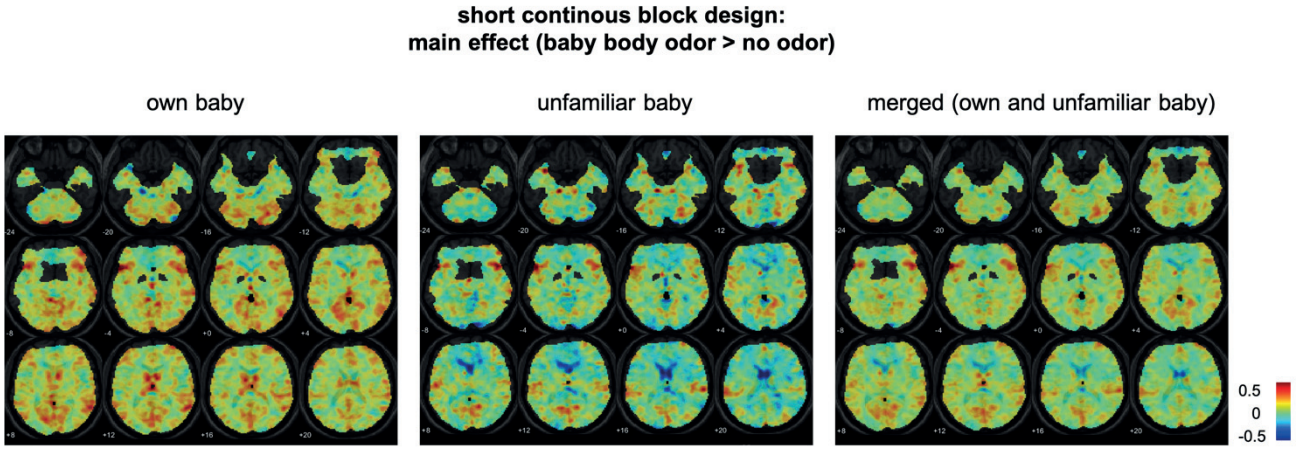
1.1 Supplementary Figures



Supplementary Figure 1. Schematic visualization of design and analysis method; and true color images depicting group results of whole brain analyses. **Left panel:** long pulsed block design: 8x on-period (á 15 seconds pulsed presentation: 1 second on, 2 seconds off), 8x off-period (á 30 seconds), analyzed with full (15 seconds; upper panel, "$long_{full}$") and reduced (7.5 seconds; panel below, "$long_{reduced}$") duration of on-period. **Right panel:** short continuous block design: 13x on-

period (á 6 seconds continuous presentation), 13x off-period (á 19 seconds) analyzed with full (13; panel above, "$short_{full}$") and reduced number of repetitions (8; panel below, "$short_{reduced}$"). True color images of group activation (n=10) are presented for different design and analysis approaches representing weighted sum of related beta values. Images are displayed from z = -24 to z = +20. Color scale ranges from negative to positive intensity.

Supplementary Figure 2.



Supplementary Figure 2. True color images of group activation (n=10) of whole brain analyses are presented for main effects of baby body odor (own, unfamiliar, merged) for the short continuous block design representing weighted sum of related beta values. Images are displayed from z = -24 to z = +20. Color scale ranges from negative to positive intensity.

2 Detailed description of body odor sampling and experimental presentation

For collecting the body odor probe of their child, subjects were equipped with a study kit. The set contained an onesie (kolibri GmbH, Waiblingen, Germany, www.koli-bri.net/startseite) in the respective size of the child, a re-closable plastic zip bag, as well as odorless medical shower gel, shampoo (both EUBOS flüssig wasch+dusch, Dr. Hobein GmbH, Meckenheim, Germany, www.eubos.de) and odorless washing powder (Denkmit Vollwaschmittel Ultra Sensitive, dm-drogerie markt GmbH & Co. KG, Karlsruhe, Germany, www.dm.de). Procedure was explained in detail and subjects received a study instructions sheet for taking home. The babies had to sleep in the onesie for one night after a standardized protocol. This included precedent washing of the sheets, blankets of the child, and clothes additionally worn to the onesie with the odorless washing powder; as well as washing the child with the odorless medical shower gel the evening before the experimental night. Parents were instructed to refrain from usage of any perfumed hygiene products.

In addition, participants received an e-mail with detailed instructions for the subsequent study procedure. After the baby slept in the onesie parents were instructed to store the onesie in the zip-closed plastic bag and to bring it back to the Lab of the Psychosomatic Department of the University Hospital Dresden the morning after the experimental night. In case the delivery would take longer than 2 hours after waking up, participants were instructed to cool the onesie until it was brought to the University Hospital. At the lab, the superior part of the onesie was cut in half and frosted by -25 °C (up to eight weeks before the trial) and defrosted 1.5 hours before starting the experiment.

For the experiment, the armpit was used and stored in glass bottles connected with teflon tubes (5 m length) to the air-dilution computer controlled olfactometer [5]. The glass bottles were warmed with an fMRI compatible heating system until body temperature was reached in order to ensure an optimal distribution of the olfactory molecules. Olfactory stimulation was delivered birhinally via a silicon nose-piece (4 mm outer diameter) connected to the teflon tubing.

Parents completed additional anamnestic, demographic assessment and standardized questionnaires via an online survey (LimeSurvey, https://bildungsportal.sachsen.de/survey/) including the following questionnaires assessing bonding (Postpartal Bonding Questionnaire, PBQ, [6]), depressive symptoms (Beck Depression Inventory, BDI-II, [7]), as well as behavioral inhibition and activation (Behavioral Inhibition Scale/Behavioral Activation Scale, BIS/BAS, [8]).

2.1 Extended sample description.

The anamnestic and demographic assessment of the participants revealed that all children were healthy and did not suffer from any diseases, as well as there were no preterm births.

Three of 10 mothers stated complications during pregnancy (gestational diabetes*, hypertension, in-patient stay due to excessive vomiting throughout pregnancy).* Two oft ten mothers reported perinatal complications (*kidney congestion*, *abdominal delivery, sudden decrease of heartbeat*). One mother stated postnatal complications (*jaundice*).

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B Weitere Veröffentlichungen während der Promotionsphase

Schäfer, L., Schellong, J., Hähner, A., Weidner, K., Hüttenbrink, K. B., Trautmann, S., ... & Croy, I. (2019). Nocturnal Olfactory Stimulation for Improvement of Sleep Quality in Patients With Posttraumatic Stress Disorder: A Randomized Exploratory Intervention Trial. *Journal of traumatic stres*s, 32(1), 130-140.

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C Konferenzbeiträge und andere Leistungen während der Promotionsphase

26. - 30. April 2017	***AChemS 2017: Annual Meeting of the Association for Chemoreception Sciences (Travelaward)*** Bonita Springs, Florida, USA Posterpräsentation
11. - 15 September 2017	***Teilnahme am Great ipid4all-Programm der Graduiertenakademie*** Forschungsaufenthalt an der Universität Linköping, Schweden Center for Social and Affective Neuroscience (CSAN) Department of Clinical and Experimental Medicine (IKE)
25. - 27. September 2017	***SPM 2017: Funktionelle Bildgebung*** Institut für Systemische Neurowissenschaften, Universitätsklinikum Hamburg-Eppendorf
10. - 12. November 2017	***DGSM 2017: Jahreskongress der Deutschen Gesellschaft für Schlafmedizin***

	Münster Kurzvortrag
01. - 02. Februar 2018	***ISATCA: International Symposium for Affective Touch in Children and Adolescents*** Dresden
23. - 24. Februar 2018	***International Lab Meeting, Smell & Taste Clinic, Prof. Thomas Hummel*** Dresden Posterpräsentation
01. - 03. März 2018	***DeGPT 2018: Jahrestagung der Deutschsprachigen Gesellschaft für Psychotraumatologie (Tagungsstipendium)*** Dresden Posterpräsentation
17. - 21. Juni 2018	***OHBM 2018: Annual Meeting of the Organization of Human Brain Mapping*** Singapur, Singapur Posterpräsentation
05. - 08. September 2018	***ECRO 2018: Annual Meeting of the European Chemoreception Research Organization*** Würzburg Vortrag
20. - 22. März 2019	***DKPM 2019: Deutscher Kongress für Psychosomatik*** Berlin Kurzvortrag
01. - 02. April 2019	***Chemical communication in humans*** ***Theo Murphy international scientific meeting of the Royal Society*** Buckinghamshire, UK Posterpräsentation
10. - 11. Mai 2019	***Tagung der Marcé-Gesellschaft für Peripartale Psychische Erkrankungen e. V.*** Solothurn, Schweiz

	Vortrag
15. Mai 2019	***Forschungs- und Weiterbildungskonferenz der Klinik und Poliklinik für Psychotherapie und Psychosomatik am Universitätsklinikum Dresden*** Dresden Vortrag
09. - 13. Juni 2019	***OHBM 2019: Annual Meeting of the Organization of Human Brain Mapping*** Rom, Italien Posterpräsentation
20. - 22. Juni 2019	***PuG 2019: 45. Jahrestagung Psychologie und Gehirn*** Dresden Posterpräsentation
09. - 12. September 2019	***paEpsy 2019: Tagung für pädagogische Psychologie und Entwicklungspsychologie (Universität Leipzig)*** Leipzig Vortrag
21. - 22. September 2019	***21. Jahrestagung der Klinik und Poliklinik für Psychotherapie und Psychosomatik am Universitätsklinikum Dresden*** Dresden Workshopleitung
24. - 27. September 2019	***PTNCE 2019: 6th International Conference of the Polish Society for Human and Evolution Studies*** Prag, Tschechien Vortrag
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II Letters of Acceptance

Von: Philosophical Transactions B <onbehalfof@manuscriptcentral.com> **Gesendet:** Donnerstag, 12. September 2019 14:40:52
An: Schäfer, Laura
Cc: philtransb@royalsociety.org; craig.roberts@stir.ac.uk

Betreff: Philosophical Transactions B - Decision on Manuscript ID RSTB-2019-0266.R2

Dear Ms Schäfer,

I am pleased to inform you that your manuscript entitled "Body odours as a chemosignal in the mother-child relationship: New insights based on an HLA-genotyped family cohort" has been approved for publication in the upcoming theme issue of Philosophical Transactions B.

The Royal Society Production Office will be in contact with you in due course, but please note all papers within an issue are published together so there may be a slight delay before you hear from them. They will contact you when the issue is ready to let you know when you should expect to receive your proofs for checking, and to update you on the publication schedule.

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On behalf also of Benoist and Jan, we thank you very much for your contribution to this issue. Yours sincerely,

Prof Craig Roberts craig.roberts@stir.ac.uk

Referee reports (where applicable):

Von: Frontiers Psychology <psychology.editorial.office@frontiersin.org>
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An: Schäfer, Laura
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Journal: Frontiers in Psychology, section Perception Science
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